

09/923,236

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(FILE 'HOME' ENTERED AT 11:45:12 ON 30 JAN 2004)

FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS, LIFESCI' ENTERED AT 11:45:38 ON 30 JAN 2004

L1 6 S "ZSIG63"  
L2 4 DUP REM L1 (2 DUPLICATES REMOVED)  
L3 146427 S SALIVARY  
L4 150 S ZSIG###  
L5 12 S L3 AND L4  
L6 8 DUP REM L5 (4 DUPLICATES REMOVED)  
L7 6346882 S CLON? OR EXPRESS? OR RECOMBINANT  
L8 126 S L4 AND L7  
L9 100 S HUMAN AND L8  
L10 23 S CANCER AND L9  
L11 23517 S TRANSCRIPTION(A) ACTIVATION OR ANTI(W) MICROBIAL  
L12 4 S L9 AND L11  
L13 23517 S L11 OR L12  
L14 26 S L12 OR L10  
L15 21 DUP REM L14 (5 DUPLICATES REMOVED)  
E ADLER D A/AU  
L16 233 S E3  
E SHEPPARD P O/AU  
L17 194 S E3  
L18 422 S L16 OR L17  
L19 49 S L4 AND L18  
L20 49 DUP REM L19 (0 DUPLICATES REMOVED)  
L21 4 S L1 AND L20  
L22 4 DUP REM L21 (0 DUPLICATES REMOVED)

=>

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=> s "zsig63"  
L1 6 "ZSIG63"

=> dup rem l1  
PROCESSING COMPLETED FOR L1  
L2 4 DUP REM L1 (2 DUPLICATES REMOVED)

=> d 1-4 ibib ab

L2 ANSWER 1 OF 4 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN  
ACCESSION NUMBER: 2003-13605 BIOTECHDS  
TITLE: Novel isolated **zsig63** polypeptide, member of the  
adhesin family, useful for treating dental carries,  
periodontal disease, thrush, gastrointestinal disease,  
urinary tract infections, vaginal infections, skin infections  
;  
vector-mediated gene transfer and expression in host cell  
for recombinant protein production for use in disease  
diagnosis and gene therapy  
AUTHOR: ADLER D A; SHEPPARD P O  
PATENT ASSIGNEE: ADLER D A; SHEPPARD P O  
PATENT INFO: US 2002173027 21 Nov 2002  
APPLICATION INFO: US 2001-922469 3 Aug 2001  
PRIORITY INFO: US 2001-922469 3 Aug 2001; US 1999-124820 17 Mar 1999  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 2003-328428 [31]  
AB DERWENT ABSTRACT:  
NOVELTY - An isolated **zsig63** polypeptide (I) comprising at

least 90 % identity to an amino acid sequence which comprises amino acids 16(Arg)-37(Ser) (domain 1 of **zsig63**), 38(Leu)-126(Ala) (domain 2), 127(Pro)-219(Gln) (domain 3), 16(Arg)-219(Gln) (mature **zsig63** polypeptide) or 1(Met)-219(Gln) of a 219 amino acid sequence (S1), given in the specification, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for: (1) an isolated polynucleotide (II) encoding (I); (2) an expression vector (III) comprising the following operably linked elements, a transcription promoter, DNA segment encoding a **zsig63** polypeptide comprising an amino acid sequence that is at least 90 % identical to amino acids 16(Arg)-219(Gln) of (S1), and a transcription terminator; (3) a cultured cell (IV) into which has been introduced (III), where the cell expresses a polypeptide encoded by the DNA segment; (4) a DNA construct (V) encoding a fusion protein, comprising a first DNA segment encoding a polypeptide chosen from amino acid sequence (S1) from residues 1(Met)-15(Ala), 16(Arg)-37(Ser), 38(Leu)-126(Ala), 127(Pro)-219(Gln), 16(Arg)-219(Gln), and at least one other DNA segment encoding an additional polypeptide, where the first and other DNA segments are connected in-frame, and encode the fusion protein; (5) a fusion protein (VI) produced by culturing a host cell into which has been introduced a vector comprising operably linked transcriptional promoter, (V), and transcriptional terminator, and recovering the protein encoded by the DNA segment; (6) producing (I); (7) detecting in a test sample, the presence of agonist of **zsig63** protein activity, comprising: (a) transfecting a **zsig63**-responsive cell with a reporter gene construct that is responsive to **zsig63**-stimulated cellular pathway, adding a test sample; and (b) comparing levels of response in the presence and absence of the test sample, by a biological or biochemical assay, and determining from the comparison, the presence of the agonist of **zsig63** activity in the sample; (8) producing an antibody to **zsig63** polypeptide, which involves inoculating an animal with a polypeptide consisting of 9-204 amino acids, which consists of a contiguous sequence of amino acids in (S1) from amino acids 16(Ala)-219(Gln), (I), and a polypeptide comprising amino acids 16(Arg)-37(Ser), 38(Leu)-126(Ala), 127(Pro)-219(Gln), 16(Arg)-219(Gln), 1(Met)-219(Gln), 14(Phe)-19(Arg), 16(Arg)-21(Phe), 24(Gly)-29(Asp), 25(Glu)-30(Asp), 187(Glu)-192(Glu), 24(Gly)-33(Pro), 17(Lys)-33(Pro), 66(Thr)-73(Pro), 103(Pro)-108(Gly), 190(Ala)-197(Glu), 202(Lys)-215(Gly) or 190(Ala)-215(Glu) of (S1), where the polypeptide elicits an immune response in the animal to produce the antibody, and isolating the antibody from the animal; (9) an antibody (VII) produced by the method of (8), which binds to (I); and (10) an antibody (VIII) that binds to (I).

WIDER DISCLOSURE - (1) counterpart polypeptides and polynucleotides of **zsig63**; (2) allelic and splice variants of (S1) and (S2); (3) functional fragments of (I) and the polynucleotides encoding the fragments; (4) identifying agonist and antagonist of **zsig63** polypeptide using a microphysiometer; and (5) mice engineered to express **zsig63** gene referred to as transgenic mice, and mice that exhibit complete absence of **zsig63** gene function referred to as knockout mice.

BIOTECHNOLOGY - Preparation: (I) is produced by culturing (IV) and isolating the polypeptide produced by the cell (claimed). Preferred Polynucleotide: (I), preferably comprises an amino acid sequence which comprises amino acid residues 16(Arg)-37(Ser), 38(Leu)-126(Ala), 127(Pro)-219(Gln), 16(Arg)-219(Gln) or 1(Met)-219(Gln) of (S1). (II) nucleotides 173-784 or 128-784 of a 1008 nucleotide sequence (S2), given in the specification, or a polynucleotide sequence complementary to the sequence. Optionally, (II) comprises nucleotides 1-657 of a fully defined degenerate sequence of (S1) which has 657 nucleotides, given in the specification. Preferred Vector: (III) further comprises a secretory signal sequence operably linked to the DNA segment. Preferred Antibody: (VII) is a monoclonal antibody.

ACTIVITY - Antimicrobial; Antibacterial; Vulnerary. No biological data is given.

#### MECHANISM OF ACTION - Gene therapy.

USE - (I) is useful for detecting in a test sample, the presence of antagonist of **zsig63** protein activity, which involves transfecting a **zsig63**-responsive cell with a reporter gene construct that is responsive to **zsig63**-stimulated cellular pathway, and producing (I) by recombinant techniques, and adding (I) to the cell in the presence and absence of the test sample, and comparing level of response to the polypeptide in the presence and absence of the test sample, by a biological or biochemical assay, and determining from the comparison, the presence of the antagonist of **zsig63** activity in the sample. (IV) is useful for producing (I) by standard recombinant methods. (All claimed.) (I) comprises 16 full evenly-spaced coil-like repeats in domain 2. The coil-like repeats are useful for identifying new family members. (I) and (II) are useful for identifying and isolating receptors that bind to **zsig63** polypeptide. (I) has antimicrobial activity and since exhibits high expression in salivary gland, can be used for treating dental carries, periodontal disease, thrush, and gastrointestinal disease, urinary tract infections, vaginal infections, skin infections and other epithelial wounds. The polypeptides can be used to establish normal microflora and protect against pathogenic colonization and invasion. (I) can also be used for providing pro-inflammatory activity for treating chronic, tissue damage particularly in areas having limited or damaged vascular system, e.g. damage in extremities associated with diabetes. (I) is also useful for treating conditions where stimulation of immune responsiveness is desired, e.g. AIDS patient or in individuals that have undergone chemotherapy, radiation treatment, etc. (I) is also useful for treating lung infections associated with cystic fibrosis. (I) is useful for studying chemoattraction of monocytes in cell culture, studying activity of melanocortin family of receptors in cell culture, studying ion flux in cell culture, studying cytotoxic activity in mammalian cell such as tumor cells in cell culture, as cell culture reagents in in vitro studies of exogenous microorganism infection such as bacterial, viral or fungal infections, and for studying epithelial cell defensin induction in cell culture. (I) is useful as a diagnostic reagent e.g. **zsig63** polypeptide is detected in the serum or tissue biopsy of a patient, for evaluating salivary gland function or dysfunction (e.g. digestive dysfunction, wound healing dysfunction, inadequate saliva production or composition, mucosal integrity breakdown, and failure or diminished anti-microbial function. Detection of **zsig63** polypeptide at relatively high levels in the trachea may indicate that such polypeptides may serve as a marker of lung dysfunction. (I) is also useful as a diagnostic reagent for conditions associated with salivary gland or lung dysfunction including salivary gland carcinoma, Pneumocystis carinii infection (particularly associated with AIDS patient), emphysema, chronic bronchitis, etc. (I) is also useful for diagnosing prostate dysfunctions such as prostate adenocarcinoma. (I) is useful for aiding digestion, and as components of defined cell culture media and may be used alone or in combination with other cytokines and hormones to replace serum that is commonly used in culture. The **zsig63** polypeptides are useful as research reagent such as for the expansion of cultured cells, and as immunogen to prepare anti-**zsig63** antibodies. (II) is useful in gene therapy applications to increase or inhibit **zsig63** activity, and for detecting abnormalities on human chromosome 4 associated with disease or other human traits. **Zsig63** polynucleotide probes can be used to detect abnormalities or genotypes associated with genes located at the 4q12-4q13 region of chromosome 4, e.g. dentinogenesis imperfecta, and dentin dysplasia type II.

ADMINISTRATION - (I) is administered by topical, inhalant, parenteral, preferably intravenous or subcutaneous delivery. No dosages is given.

EXAMPLE - Scanning of a translated DNA database resulted in identification of an expressed sequence tag (EST) sequence found to be a novel member of the adhesin family and designated **zsig63**.

Confirmation of the EST sequence was made by sequence analyses of the cDNA from which the EST originated. This cDNA clone was obtained and sequenced. Northern blot tissue distribution of the mRNA revealed high expression in salivary gland, and moderate to high expression in thyroid. (32 pages)

L2 ANSWER 2 OF 4 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN

ACCESSION NUMBER: 2003-01837 BIOTECHDS

TITLE: Novel secreted salivary polypeptide, **zsig63**, useful as antimicrobial agent for treating microbial infection, dental carries, periodontal disease, thrush gastrointestinal disease, and for aiding digestion; recombinant protein production and agonist and antagonist use in disease therapy and gene therapy

AUTHOR: ADLER D A; SHEPPARD P O

PATENT ASSIGNEE: ADLER D A; SHEPPARD P O

PATENT INFO: US 2002090677 11 Jul 2002

APPLICATION INFO: US 2001-923236 3 Aug 2001

PRIORITY INFO: US 2001-923236 3 Aug 2001; US 1999-124820 17 Mar 1999

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2002-642378 [69]

AB DERWENT ABSTRACT:

NOVELTY - An isolated secreted salivary polypeptide (I) designated as **zsig63**, comprising an amino acid sequence 90% identical to a sequence (S1) of 1 (Met)-219 (Gln) fully defined in the specification, 16 (Arg)-37 (Ser), 38 (Leu)-126 (Ala), 127 (Pro)-219 (Gln) or 16 (Arg)-219 (Gln) of (S1), is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) an isolated polynucleotide (II) encoding (I); (2) an expression vector (III) comprising a transcription promoter, a DNA segment encoding a **zsig63** polypeptide comprising an amino acid sequence that is 90% identical to (S1) from amino acid 16 (Arg)-219 (Gln) and a transcription terminator, operably linked to each other; (3) a cultured cell (IV) containing (III), expresses a polypeptide encoded by the DNA segment; (4) a DNA construct (V) encoding a fusion protein, comprises a first DNA segment encoding a polypeptide comprising an amino acid sequence of 1 (Met)-15 (Ala), 16 (Arg)-37 (Ser), 38 (Leu)-126 (Ala), 127 (Pro)-219 (Gln) or 16 (Arg)-219 (Gln) of (S1), and at least one other DNA segment encoding an additional polypeptide, where the first and other DNA segments are connected in-frame and encode the fusion protein; (5) a fusion protein produced by culturing a host cell comprising a vector having transcriptional promoter, (V), a transcriptional terminator, operably linked to each other and recovering the protein encoded by the DNA segment, is introduced; (6) producing (I); (7) detecting in a test sample, the presence of an agonist or antagonist of **zsig63** protein activity, involves transfecting a **zsig63**-responsive cell, with a reporter gene construct that is responsive to a **zsig63**-stimulated cellular pathway and producing a **zsig63** polypeptide by the culturing the cell, and adding the **zsig63** polypeptide to the cell in the presence and absence of a test sample and comparing levels of response to the **zsig63** polypeptide, in the presence and absence of the test sample, by a biological or biochemical assay and determining from the comparison, the presence of the agonist or antagonist of **zsig63** activity in the test sample; (8) producing an antibody to **zsig63** polypeptide, involves inoculating animal with polypeptides consisting of 9 to 204 amino acids, the polypeptide consist of a contiguous sequence of amino acids in (S1) from amino acid 16 (Ala) to amino acid number 219 (Gln), (I), or a polynucleotide comprising 14 (Phe)-19 (Arg), 16 (Arg)-21 (Phe), 24 (Gly)-29 (Asp), 25 (Glu)-30 (Asp), 187 (Glu)-192 (Glu), 24 (Gly)-33 (Pro), 17 (Lys)-33 (Pro), 66 (Thr)-73 (Pro), 102 (Pro)-108 (Gly), 180 (Ala)-197 (Glu), 202 (Lys)-215 (Gly), 190 (Ala)-215 (Glu) of (S1), where the polypeptide elicits an immune response in the animal to produce the antibody, and

isolating the antibody from the animal; and (9) an antibody (Ab) produced by the above method which binds to a **zsig63** polypeptide or (I).

WIDER DISCLOSURE - Also disclosed are: (1) a **zig63** polypeptide-encoding polynucleotides comprising a sequence of 657 nucleotides fully defined in the specification; (2) fragments of a sequence of 1008 nucleotides fully defined in the specification; (3) orthologs, variant or functional fragment of (I) and (II); (4) nucleic acid molecule encoding functional fragment of (I); (5) a pharmaceutical composition comprising (I); and (6) reagent comprising **zsig63** gene, a probe comprising **zsig63** DNA or RNA or a subsequence for diagnostic application.

BIOTECHNOLOGY - Preparation: (I) is produced by culturing (IV) and isolating (I) produced by the cell. Preferred Vector: (III) further comprises a secretory signal sequence operably linked to the DNA segment. Preferred Antibody: Ab is a monoclonal antibody.

ACTIVITY - Antibacterial; Fungicide; Virucide; Antiinflammatory; Antiarteriosclerotic; Vasotropic; Anorectic. No biological data provided.

MECHANISM OF ACTION - Gene therapy; Modulator of (I). No supporting data provided.

USE - (I) is useful as a host defense polypeptide, immune modulating factor, antipathogenic polypeptide, cell-cell signaling molecule, growth factor, cytokine, or as secreted extracellular matrix associated proteins with growth factor hormone activity. (I) is useful for treating conditions associated with pathological microbes, including bacterial, fungal, and viral infections, for treating dental carries (tooth decay), periodontal disease, thrush, and gastrointestinal disease, for treating urinary tract infection, vaginal infection, and for preventing infection in skin and other epithelial wounds. (I) is useful for establishing normal microflora and protect against pathogenic colonization and invasion, for treating chronic tissue damage e.g. damage in extremities associated with diabetes, and useful as anti-inflammatory agents. (I) is useful as a marker of lung dysfunction, salivary gland dysfunction, or dysfunction of prostate gland. (I) is therapeutically useful for aiding digestion. (I) is useful as a research reagent for the expansion of cultured cells, to prepare antibodies that bind to **zsig63** epitopes, peptides or polypeptides, as antigen to inoculate an animal for eliciting an immune response. **zsig63** is useful for identifying cells, tissues or cell lines which respond to **zsig63**-stimulated pathway, or for identifying inhibitors of its activity. (I) is useful for studies to isolate mesenchymal stem cells and myocyte or other progenitor cells both in vivo and ex vivo, and serve as an additional cell surface or secreted marker associated with stage-specific expression of a tissue. (II) is useful in gene therapy for increasing or inhibiting **zsig63** activity, for detecting abnormalities on human chromosome 4 associated with disease or other human traits and as diagnostics in forensic DNA profiling. (I) or Ab is useful for studying chemoattraction of monocytes, for studying the activity of the melanocortin family of receptors, for studying or evaluating ligand or putative ligand binding and/or ion flux (calcium flux, potassium flux, sodium flux) regulation or modulation, for studying cytotoxic activity against mammalian cells, as cell culture reagent in in vitro studies of exogenous microorganism infection, and in in vivo animal models of infection. (I) or Ab is useful for identifying and isolating receptors for **zsig63**. Ab is useful for detecting **zsig63** polypeptides in the serum or tissue biopsy of a patient undergoing evaluation for salivary gland function or dysfunction. Ab is useful for tagging cells that express **zsig63**, for isolating **zsig63** for diagnostic assays for determining circulating levels of **zsig63** polypeptides, for detecting or quantitating soluble **zsig63** as marker of underlying pathology or disease, in analytical methods employing fluorescence activated cell sorting (FACS), for screening expression libraries, for generating anti-idiotypic antibodies, as neutralizing antibodies or as antagonists to block **zsig63** activity in vitro or in vivo, and in in vitro detection of denatured **zsig63** or its fragments in assays. (I),

(II) or Ab is useful for stimulating proliferation or differentiation of cardiac myocytes, for proliferation or differentiation of adipocytes and for inhibiting chondrosarcomas, atherosclerosis, restenosis and obesity.

ADMINISTRATION - Pharmaceutical composition comprising (I) is administered through topical, inhalation, parenteral, intravenous or subcutaneous route. Dosage not specified.

EXAMPLE - Full-length **zsig63** was obtained using an expressed sequence tag (EST) sequence. Scanning of a translated DNA database resulted in identification of EST sequence found to be a novel member of the adhesion family and designated **zsig63**. Confirmation of EST sequence was made by sequence analyses of the cDNA from the EST originated. This cDNA clone was obtained and sequenced using the ZC6768 (gcaattaaccctcactaaaggggaac), ZC694 (taatacgactcactatagggg), ZC7231 (tttttttttttttttttttttttttttttv), ZC7764a (tttttttttttttttttttttttttta). The insert was about 1 kb and was full-length. (33 pages)

L2 ANSWER 3 OF 4 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN

ACCESSION NUMBER: 2003-01808 BIOTECHDS

TITLE: Novel secreted salivary protein, **zsig63** and polynucleotide encoding it useful for treating microbial infections, inflammatory conditions, dental caries and lung infections associated with cystic fibrosis; vector-mediated gene transfer and expression in host cell for recombinant protein production, drug screening and gene therapy

AUTHOR: ADLER D A; SHEPPARD P O

PATENT ASSIGNEE: ADLER D A; SHEPPARD P O

PATENT INFO: US 2002081701 27 Jun 2002

APPLICATION INFO: US 2001-922480 3 Aug 2001

PRIORITY INFO: US 2001-922480 3 Aug 2001; US 1999-124820 17 Mar 1999

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2002-635468 [68]

AB DERWENT ABSTRACT:

NOVELTY - An isolated **zsig63** (I), a secreted salivary protein comprising a sequence of amino acid residues that is at least 90% identical to a sequence (S1) of 219 amino acids given in the specification, or amino acids 16-37, 38-126, 127-219 or 16-219 of (S1), is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) an isolated polynucleotide (II) encoding (I); (2) an expression vector (III) comprising a DNA segment encoding **zsig63** polypeptide comprising an amino acid sequence that is 90% identical to amino acids 16-219 of (S1), and transcription promoter and terminator; (3) a cultured cell (IV) into which has been introduced (III), where the cell expresses a polypeptide encoded by the DNA segment; (4) a DNA construct encoding a fusion protein, comprising a first DNA segment encoding amino acids 1-15, 16-37, 38-126, 127-219 or 16-219 of (S1), and at least one other DNA segment encoding an additional polypeptide, where the first and other DNA segments are connected in-frame and encode the fusion protein; (5) a fusion protein produced by culturing a host cell into which has been introduced a vector comprising the above DNA construct and transcription promoter and terminator; (6) producing **zsig63** polypeptide; and (7) an antibody (V) produced using (I), that binds to (I).

BIOTECHNOLOGY - Preparation: (I) is produced by culturing (IV) and isolating the polypeptide produced by the cell (claimed). Preferred Polypeptide: (I) comprises amino acids 16-37, 38-126, 127-219, 16-219 or 1-219 of (S1). Preferred Polynucleotide: (II) comprises a polynucleotide sequence (or its complement) comprising nucleotides 173-784 or 128-784 of a sequence (S2) of 1008 bp given in the specification. Preferred Vector: (III) further comprises a secretory signal sequence operably linked to the DNA segment. Preferred Antibody: (V) is a monoclonal antibody.



ACTIVITY - Antibacterial; Fungicide; Virucide; Vulnerary; Anti-HIV; Antiinflammatory. No supporting data given.

MECHANISM OF ACTION - Gene therapy. No supporting data given.

USE - (I) is useful for detecting in a test sample, the presence of an antagonist or agonist of **zsig63** protein activity. The method comprises transfecting a **zsig63**-responsive cell with a reporter gene construct that is responsive to a **zsig63**-stimulated cellular pathway, adding the **zsig63** polypeptide to the cell, in the presence and absence of the test sample, comparing the levels of response to the **zsig63** polypeptide in the presence and absence of the test sample, by a biological or biochemical assay, and determining from the comparison, the presence of the antagonist or agonist of **zsig63** activity in the test sample. (I) is also useful as an immunogen for producing an antibody to **zsig63** polypeptide, by inoculating an animal with (I), or its fragment comprising amino acids 9-204, 14-19, 16-21, 24-29, 25-30, 187-192, 24-33, 17-33, 66-73, 103-108, 190-197, 202-215, or 190-215 of (S1) and isolating the antibody from the animal (all claimed). **zsig63**-cytokine fusion proteins or antibody-cytokine fusion protein are useful for enhancing in vivo killing of target tissues. Pharmaceutical composition comprising purified **zsig63** polypeptide are useful in the treatment of conditions associated with pathological microbes, including bacterial, fungal and viral infections. High expression of **zsig63** in salivary gland suggests that anti-microbial polypeptides are useful for treatment of dental caries (tooth decay), periodontal disease, thrush and gastrointestinal disease. Other applications can be used in urinary tract infections, vaginal infections, prevention of infection in skin and other epithelial wounds. The polypeptides can be used to establish normal microflora and protect against pathogenic colonization and invasion. (I) is useful when pro-inflammatory activity is desired. Applications for such pro-inflammatory activity include the treatment of chronic tissue damage, particularly in areas having a limited or damaged vascular system e.g., damage in extremities associated with diabetes. Antagonists to **zsig63** polypeptides may be useful as anti-inflammatory agents. (I) is useful for the treatment of patients having incompetent immune system, such as AIDS patients or individuals that have undergone chemotherapy, radiation treatment. (I) is also useful for the treatment of lung infections associated with cystic fibrosis, for studying chemoattraction of monocytes in cell culture, for studying activity of the melanocortin family of receptors and ion flux in cell culture, and cytotoxic activity against mammalian cells. (I), its fragments, fusion proteins, or agonists are useful as cell culture reagents in in vitro studies of exogenous microorganism infection, such as bacterial, viral or fungal infection and also in in vivo animal models of infection. (I), its agonists or antagonists are useful for aiding digestion. **zsig63** is also useful to identify cells, tissues or cell lines which respond to a **zsig63**-stimulated pathway, to identify and isolate receptors for **zsig63** and in diagnostic applications. The diagnostic methods are useful in genetic linkage analysis, to detect a genetic abnormality or aberration in a patient. (V) is useful for detecting **zsig63** polypeptides.

ADMINISTRATION - Administered by topical, inhalant or parenteral, particularly intravenous or subcutaneous route. Dosage not specified.

EXAMPLE - Scanning of a translated DNA database resulted in identification of an expressed sequence tag (EST) sequence found to be a novel member of the adhesion family and designated **zsig63**. Confirmation of the EST sequence was made by sequence analyses of 25 the cDNA from which the EST originated. This cDNA clone was obtained and sequenced using the following primers ZC6768 (gcaattaaccctcactaaaggggaac, ZC694 (taatacgaactcactataggg), ZC7231 (ttttttttttttttttttttttttttv) and ZC7764a (tttttttttttttttttttttttta). The insert was about 1 kb and was full-length. **zsig63** was mapped to chromosome 4. (33 pages)

DUPLICATE 1

ACCESSION NUMBER: 2002:143438 BIOSIS  
 DOCUMENT NUMBER: PREV200200143438  
 TITLE: Secreted salivary **ZSIG63** Polypeptide.  
 AUTHOR(S): Adler, David A. [Inventor, Reprint author]; Sheppard, Paul O. [Inventor]  
 CORPORATE SOURCE: Bainbridge Island, WA, USA  
 ASSIGNEE: ZymoGenetics, Inc.  
 PATENT INFORMATION: US 6331413 December 18, 2001  
 SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Dec. 18, 2001) Vol. 1253, No. 3.  
<http://www.uspto.gov/web/menu/patdata.html>. e-file.  
 CODEN: OGUPE7. ISSN: 0098-1133.  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 ENTRY DATE: Entered STN: 14 Feb 2002  
 Last Updated on STN: 26 Feb 2002

AB The present invention relates to polynucleotide and polypeptide molecules for **zsig63**, a novel secreted salivary protein. The polypeptides, and polynucleotides encoding them, may exhibit anti-microbial activity and may be used in the study or treatment of microbial infections. The polynucleotides encoding **zsig63**, are located on chromosome 4, and can be used to identify a region of the genome associated with human disease states. The present invention also includes antibodies to the **zsig63** polypeptides.

=> s salivary

L3 146427 SALIVARY

=> s Zsig###

L4 150 ZSIG###

=> s l3 and l4

L5 12 L3 AND L4

=> dup rem l5

PROCESSING COMPLETED FOR L5

L6 8 DUP REM L5 (4 DUPLICATES REMOVED)

=> d 1-8 ibib ab

L6 ANSWER 1 OF 8 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN

ACCESSION NUMBER: 2003-13605 BIOTECHDS

TITLE: Novel isolated **zsig63** polypeptide, member of the adhesin family, useful for treating dental carries, periodontal disease, thrush, gastrointestinal disease, urinary tract infections, vaginal infections, skin infections

;

vector-mediated gene transfer and expression in host cell for recombinant protein production for use in disease diagnosis and gene therapy

AUTHOR: ADLER D A; SHEPPARD P O

PATENT ASSIGNEE: ADLER D A; SHEPPARD P O

PATENT INFO: US 2002173027 21 Nov 2002

APPLICATION INFO: US 2001-922469 3 Aug 2001

PRIORITY INFO: US 2001-922469 3 Aug 2001; US 1999-124820 17 Mar 1999

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2003-328428 [31]

AB DERWENT ABSTRACT:

NOVELTY - An isolated **zsig63** polypeptide (I) comprising at least 90 % identity to an amino acid sequence which comprises amino acids 16(Arg)-37(Ser) (domain 1 of **zsig63**), 38(Leu)-126(Ala) (domain

2), 127(Pro)-219(Gln) (domain 3), 16(Arg)-219(Gln) (mature **zsig63** polypeptide) or 1(Met)-219(Gln) of a 219 amino acid sequence (S1), given in the specification, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for: (1) an isolated polynucleotide (II) encoding (I); (2) an expression vector (III) comprising the following operably linked elements, a transcription promoter, DNA segment encoding a **zsig63** polypeptide comprising an amino acid sequence that is at least 90 % identical to amino acids 16(Arg)-219(Gln) of (S1), and a transcription terminator; (3) a cultured cell (IV) into which has been introduced (III), where the cell expresses a polypeptide encoded by the DNA segment; (4) a DNA construct (V) encoding a fusion protein, comprising a first DNA segment encoding a polypeptide chosen from amino acid sequence (S1) from residues 1(Met)-15(Ala), 16(Arg)-37(Ser), 38(Leu)-126(Ala), 127(Pro)-219(Gln), 16(Arg)-219(Gln), and at least one other DNA segment encoding an additional polypeptide, where the first and other DNA segments are connected in-frame, and encode the fusion protein; (5) a fusion protein (VI) produced by culturing a host cell into which has been introduced a vector comprising operably linked transcriptional promoter, (V), and transcriptional terminator, and recovering the protein encoded by the DNA segment; (6) producing (I); (7) detecting in a test sample, the presence of agonist of **zsig63** protein activity, comprising: (a) transfecting a **zsig63**-responsive cell with a reporter gene construct that is responsive to **zsig63**-stimulated cellular pathway, adding a test sample; and (b) comparing levels of response in the presence and absence of the test sample, by a biological or biochemical assay, and determining from the comparison, the presence of the agonist of **zsig63** activity in the sample; (8) producing an antibody to **zsig63** polypeptide, which involves inoculating an animal with a polypeptide consisting of 9-204 amino acids, which consists of a contiguous sequence of amino acids in (S1) from amino acids 16(Ala)-219(Gln), (I), and a polypeptide comprising amino acids 16(Arg)-37(Ser), 38(Leu)-126(Ala), 127(Pro)-219(Gln), 16(Arg)-219(Gln), 1(Met)-219(Gln), 14(Phe)-19(Arg), 16(Arg)-21(Phe), 24(Gly)-29(Asp), 25(Glu)-30(Asp), 187(Glu)-192(Glu), 24(Gly)-33(Pro), 17(Lys)-33(Pro), 66(Thr)-73(Pro), 103(Pro)-108(Gly), 190(Ala)-197(Glu), 202(Lys)-215(Gly) or 190(Ala)-215(Glu) of (S1), where the polypeptide elicits an immune response in the animal to produce the antibody, and isolating the antibody from the animal; (9) an antibody (VII) produced by the method of (8), which binds to (I); and (10) an antibody (VIII) that binds to (I).

WIDER DISCLOSURE - (1) counterpart polypeptides and polynucleotides of **zsig63**; (2) allelic and splice variants of (S1) and (S2); (3) functional fragments of (I) and the polynucleotides encoding the fragments; (4) identifying agonist and antagonist of **zsig63** polypeptide using a microphysiometer; and (5) mice engineered to express **zsig63** gene referred to as transgenic mice, and mice that exhibit complete absence of **zsig63** gene function referred to as knockout mice.

BIOTECHNOLOGY - Preparation: (I) is produced by culturing (IV) and isolating the polypeptide produced by the cell (claimed). Preferred Polynucleotide: (I), preferably comprises an amino acid sequence which comprises amino acid residues 16(Arg)-37(Ser), 38(Leu)-126(Ala), 127(Pro)-219(Gln), 16(Arg)-219(Gln) or 1(Met)-219(Gln) of (S1). (II) nucleotides 173-784 or 128-784 of a 1008 nucleotide sequence (S2), given in the specification, or a polynucleotide sequence complementary to the sequence. Optionally, (II) comprises nucleotides 1-657 of a fully defined degenerate sequence of (S1) which has 657 nucleotides, given in the specification. Preferred Vector: (III) further comprises a secretory signal sequence operably linked to the DNA segment. Preferred Antibody: (VII) is a monoclonal antibody.

ACTIVITY - Antimicrobial; Antibacterial; Vulnerary. No biological data is given.

MECHANISM OF ACTION - Gene therapy.

USE - (I) is useful for detecting in a test sample, the presence of

antagonist of **zsig63** protein activity, which involves transfecting a **zsig63**-responsive cell with a reporter gene construct that is responsive to **zsig63**-stimulated cellular pathway, and producing (I) by recombinant techniques, and adding (I) to the cell in the presence and absence of the test sample, and comparing level of response to the polypeptide in the presence and absence of the test sample, by a biological or biochemical assay, and determining from the comparison, the presence of the antagonist of **zsig63** activity in the sample. (IV) is useful for producing (I) by standard recombinant methods. (All claimed.) (I) comprises 16 full evenly-spaced coil-like repeats in domain 2. The coil-like repeats are useful for identifying new family members. (I) and (II) are useful for identifying and isolating receptors that bind to **zsig63** polypeptide. (I) has antimicrobial activity and since exhibits high expression in **salivary** gland, can be used for treating dental carries, periodontal disease, thrush, and gastrointestinal disease, urinary tract infections, vaginal infections, skin infections and other epithelial wounds. The polypeptides can be used to establish normal microflora and protect against pathogenic colonization and invasion. (I) can also be used for providing pro-inflammatory activity for treating chronic, tissue damage particularly in areas having limited or damaged vascular system, e.g. damage in extremities associated with diabetes. (I) is also useful for treating conditions where stimulation of immune responsiveness is desired, e.g. AIDS patient or in individuals that have undergone chemotherapy, radiation treatment, etc. (I) is also useful for treating lung infections associated with cystic fibrosis. (I) is useful for studying chemoattraction of monocytes in cell culture, studying activity of melanocortin family of receptors in cell culture, studying ion flux in cell culture, studying cytotoxic activity in mammalian cell such as tumor cells in cell culture, as cell culture reagents in in vitro studies of exogenous microorganism infection such as bacterial, viral or fungal infections, and for studying epithelial cell defensin induction in cell culture. (I) is useful as a diagnostic reagent e.g. **zsig63** polypeptide is detected in the serum or tissue biopsy of a patient, for evaluating **salivary** gland function or dysfunction (e.g. digestive dysfunction, wound healing dysfunction, inadequate saliva production or composition, mucosal integrity breakdown, and failure or diminished anti-microbial function. Detection of **zsig63** polypeptide at relatively high levels in the trachea may indicate that such polypeptides may serve as a marker of lung dysfunction. (I) is also useful as a diagnostic reagent for conditions associated with **salivary** gland or lung dysfunction including **salivary** gland carcinoma, Pneumocystis carinii infection (particularly associated with AIDS patient), emphysema, chronic bronchitis, etc. (I) is also useful for diagnosing prostate dysfunctions such as prostate adenocarcinoma. (I) is useful for aiding digestion, and as components of defined cell culture media and may be used alone or in combination with other cytokines and hormones to replace serum that is commonly used in culture. The **zsig63** polypeptides are useful as research reagent such as for the expansion of cultured cells, and as immunogen to prepare anti-**zsig63** antibodies. (II) is useful in gene therapy applications to increase or inhibit **zsig63** activity, and for detecting abnormalities on human chromosome 4 associated with disease or other human traits. **Zsig63** polynucleotide probes can be used to detect abnormalities or genotypes associated with genes located at the 4q12-4q13 region of chromosome 4, e.g. dentinogenesis imperfecta, and dentin dysplasia type II.

ADMINISTRATION - (I) is administered by topical, inhalant, parenteral, preferably intravenous or subcutaneous delivery. No dosages is given.

EXAMPLE - Scanning of a translated DNA database resulted in identification of an expressed sequence tag (EST) sequence found to be a novel member of the adhesin family and designated **zsig63**. Confirmation of the EST sequence was made by sequence analyses of the

cDNA from which the EST originated. This cDNA clone was obtained and sequenced. Northern blot tissue distribution of the mRNA revealed high expression in **salivary** gland, and moderate to high expression in thyroid. (32 pages)

L6 ANSWER 2 OF 8 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN

ACCESSION NUMBER: 2003-01837 BIOTECHDS

TITLE: Novel secreted **salivary** polypeptide, **zsig63**  
, useful as antimicrobial agent for treating microbial infection, dental carries, periodontal disease, thrush gastrointestinal disease, and for aiding digestion;  
recombinant protein production and agonist and antagonist use in disease therapy and gene therapy

AUTHOR: ADLER D A; SHEPPARD P O

PATENT ASSIGNEE: ADLER D A; SHEPPARD P O

PATENT INFO: US 2002090677 11 Jul 2002

APPLICATION INFO: US 2001-923236 3 Aug 2001

PRIORITY INFO: US 2001-923236 3 Aug 2001; US 1999-124820 17 Mar 1999

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2002-642378 [69]

AB DERWENT ABSTRACT:

NOVELTY - An isolated secreted **salivary** polypeptide (I) designated as **zsig63**, comprising an amino acid sequence 90% identical to a sequence (S1) of 1 (Met)-219 (Gln) fully defined in the specification, 16 (Arg)-37 (Ser), 38 (Leu)-126 (Ala), 127 (Pro)-219 (Gln) or 16 (Arg)-219 (Gln) of (S1), is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) an isolated polynucleotide (II) encoding (I); (2) an expression vector (III) comprising a transcription promoter, a DNA segment encoding a **zsig63** polypeptide comprising an amino acid sequence that is 90% identical to (S1) from amino acid 16 (Arg)-219 (Gln) and a transcription terminator, operably linked to each other; (3) a cultured cell (IV) containing (III), expresses a polypeptide encoded by the DNA segment; (4) a DNA construct (V) encoding a fusion protein, comprises a first DNA segment encoding a polypeptide comprising an amino acid sequence of 1 (Met)-15 (Ala), 16 (Arg)-37 (Ser), 38 (Leu)-126 (Ala), 127 (Pro)-219 (Gln) or 16 (Arg)-219 (Gln) of (S1), and at least one other DNA segment encoding an additional polypeptide, where the first and other DNA segments are connected in-frame and encode the fusion protein; (5) a fusion protein produced by culturing a host cell comprising a vector having transcriptional promoter, (V), a transcriptional terminator, operably linked to each other and recovering the protein encoded by the DNA segment, is introduced; (6) producing (I); (7) detecting in a test sample, the presence of an agonist or antagonist of **zsig63** protein activity, involves transfecting a **zsig63**-responsive cell, with a reporter gene construct that is responsive to a **zsig63**-stimulated cellular pathway and producing a **zsig63** polypeptide by the culturing the cell, and adding the **zsig63** polypeptide to the cell in the presence and absence of a test sample and comparing levels of response to the **zsig63** polypeptide, in the presence and absence of the test sample, by a biological or biochemical assay and determining from the comparison, the presence of the agonist or antagonist of **zsig63** activity in the test sample; (8) producing an antibody to **zsig63** polypeptide, involves inoculating animal with polypeptides consisting of 9 to 204 amino acids, the polypeptide consist of a contiguous sequence of amino acids in (S1) from amino acid 16 (Ala) to amino acid number 219 (Gln), (I), or a polynucleotide comprising 14 (Phe)-19 (Arg), 16 (Arg)-21 (Phe), 24 (Gly)-29 (Asp), 25 (Glu)-30 (Asp), 187 (Glu)-192 (Glu), 24 (Gly)-33 (Pro), 17 (Lys)-33 (Pro), 66 (Thr)-73 (Pro), 102 (Pro)-108 (Gly), 180 (Ala)-197 (Glu), 202 (Lys)-215 (Gly), 190 (Ala)-215 (Glu) of (S1), where the polypeptide elicits an immune response in the animal to produce the antibody, and isolating the antibody from the animal; and (9) an antibody (Ab) produced

by the above method which binds to a **zsig63** polypeptide or (I).

WIDER DISCLOSURE - Also disclosed are: (1) a **zig63** polypeptide-encoding polynucleotides comprising a sequence of 657 nucleotides fully defined in the specification; (2) fragments of a sequence of 1008 nucleotides fully defined in the specification; (3) orthologs, variant or functional fragment of (I) and (II); (4) nucleic acid molecule encoding functional fragment of (I); (5) a pharmaceutical composition comprising (I); and (6) reagent comprising **zsig63** gene, a probe comprising **zsig63** DNA or RNA or a subsequence for diagnostic application.

BIOTECHNOLOGY - Preparation: (I) is produced by culturing (IV) and isolating (I) produced by the cell. Preferred Vector: (III) further comprises a secretory signal sequence operably linked to the DNA segment. Preferred Antibody: Ab is a monoclonal antibody.

ACTIVITY - Antibacterial; Fungicide; Virucide; Antiinflammatory; Antiarteriosclerotic; Vasotropic; Anorectic. No biological data provided.

MECHANISM OF ACTION - Gene therapy; Modulator of (I). No supporting data provided.

USE - (I) is useful as a host defense polypeptide, immune modulating factor, antipathogenic polypeptide, cell-cell signaling molecule, growth factor, cytokine, or as secreted extracellular matrix associated proteins with growth factor hormone activity. (I) is useful for treating conditions associated with pathological microbes, including bacterial, fungal, and viral infections, for treating dental carries (tooth decay), periodontal disease, thrush, and gastrointestinal disease, for treating urinary tract infection, vaginal infection, and for preventing infection in skin and other epithelial wounds. (I) is useful for establishing normal microflora and protect against pathogenic colonization and invasion, for treating chronic tissue damage e.g. damage in extremities associated with diabetes, and useful as anti-inflammatory agents. (I) is useful as a marker of lung dysfunction, **salivary** gland dysfunction, or dysfunction of prostate gland. (I) is therapeutically useful for aiding digestion. (I) is useful as a research reagent for the expansion of cultured cells, to prepare antibodies that bind to **zsig63** epitopes, peptides or polypeptides, as antigen to inoculate an animal for eliciting an immune response. **zsig63** is useful for identifying cells, tissues or cell lines which respond to **zsig63**-stimulated pathway, or for identifying inhibitors of its activity. (I) is useful for studies to isolate mesenchymal stem cells and myocyte or other progenitor cells both in vivo and ex vivo, and serve as an additional cell surface or secreted marker associated with stage-specific expression of a tissue. (II) is useful in gene therapy for increasing or inhibiting **zsig63** activity, for detecting abnormalities on human chromosome 4 associated with disease or other human traits and as diagnostics in forensic DNA profiling. (I) or Ab is useful for studying chemoattraction of monocytes, for studying the activity of the melanocortin family of receptors, for studying or evaluating ligand or putative ligand binding and/or ion flux (calcium flux, potassium flux, sodium flux) regulation or modulation, for studying cytotoxic activity against mammalian cells, as cell culture reagent in in vitro studies of exogenous microorganism infection, and in in vivo animal models of infection. (I) or Ab is useful for identifying and isolating receptors for **zsig63**. Ab is useful for detecting **zsig63** polypeptides in the serum or tissue biopsy of a patient undergoing evaluation for **salivary** gland function or dysfunction. Ab is useful for tagging cells that express **zsig63**, for isolating **zsig63** for diagnostic assays for determining circulating levels of **zsig63** polypeptides, for detecting or quantitating soluble **zsig63** as marker of underlying pathology or disease, in analytical methods employing fluorescence activated cell sorting (FACS), for screening expression libraries, for generating anti-idiotypic antibodies, as neutralizing antibodies or as antagonists to block **zsig63** activity in vitro or in vivo, and in in vitro detection of denatured **zsig63** or its fragments in assays. (I), (II) or Ab is

useful for stimulating proliferation or differentiation of cardiac myocytes, for proliferation or differentiation of adipocytes and for inhibiting chondrosarcomas, atherosclerosis, restenosis and obesity.

ADMINISTRATION - Pharmaceutical composition comprising (I) is administered through topical, inhalation, parenteral, intravenous or subcutaneous route. Dosage not specified.

EXAMPLE - Full-length **zsig63** was obtained using an expressed sequence tag (EST) sequence. Scanning of a translated DNA database resulted in identification of EST sequence found to be a novel member of the adhesion family and designated **zsig63**. Confirmation of EST sequence was made by sequence analyses of the cDNA from the EST originated. This cDNA clone was obtained and sequenced using the ZC6768 (gcaattaaccctcactaaaggggaac), ZC694 (taatacgactcactatagggg), ZC7231 (tttttttttttttttttttttttttttttv), ZC7764a (tttttttttttttttttttttttttta). The insert was about 1 kb and was full-length. (33 pages)

L6 ANSWER 3 OF 8 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN

ACCESSION NUMBER: 2003-01808 BIOTECHDS

TITLE: Novel secreted **salivary** protein, **zsig63**  
and polynucleotide encoding it useful for treating microbial infections, inflammatory conditions, dental caries and lung infections associated with cystic fibrosis;  
vector-mediated gene transfer and expression in host cell for recombinant protein production, drug screening and gene therapy

AUTHOR: ADLER D A; SHEPPARD P O

PATENT ASSIGNEE: ADLER D A; SHEPPARD P O

PATENT INFO: US 2002081701 27 Jun 2002

APPLICATION INFO: US 2001-922480 3 Aug 2001

PRIORITY INFO: US 2001-922480 3 Aug 2001; US 1999-124820 17 Mar 1999

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2002-635468 [68]

AB DERWENT ABSTRACT:

NOVELTY - An isolated **zsig63** (I), a secreted **salivary** protein comprising a sequence of amino acid residues that is at least 90% identical to a sequence (S1) of 219 amino acids given in the specification, or amino acids 16-37, 38-126, 127-219 or 16-219 of (S1), is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) an isolated polynucleotide (II) encoding (I); (2) an expression vector (III) comprising a DNA segment encoding **zsig63** polypeptide comprising an amino acid sequence that is 90% identical to amino acids 16-219 of (S1), and transcription promoter and terminator; (3) a cultured cell (IV) into which has been introduced (III), where the cell expresses a polypeptide encoded by the DNA segment; (4) a DNA construct encoding a fusion protein, comprising a first DNA segment encoding amino acids 1-15, 16-37, 38-126, 127-219 or 16-219 of (S1), and at least one other DNA segment encoding an additional polypeptide, where the first and other DNA segments are connected in-frame and encode the fusion protein; (5) a fusion protein produced by culturing a host cell into which has been introduced a vector comprising the above DNA construct and transcription promoter and terminator; (6) producing **zsig63** polypeptide; and (7) an antibody (V) produced using (I), that binds to (I).

BIOTECHNOLOGY - Preparation: (I) is produced by culturing (IV) and isolating the polypeptide produced by the cell (claimed). Preferred Polypeptide: (I) comprises amino acids 16-37, 38-126, 127-219, 16-219 or 1-219 of (S1). Preferred Polynucleotide: (II) comprises a polynucleotide sequence (or its complement) comprising nucleotides 173-784 or 128-784 of a sequence (S2) of 1008 bp given in the specification. Preferred Vector: (III) further comprises a secretory signal sequence operably linked to the DNA segment. Preferred Antibody: (V) is a monoclonal antibody.

ACTIVITY - Antibacterial; Fungicide; Virucide; Vulnerary; Anti-HIV; Antiinflammatory. No supporting data given.

MECHANISM OF ACTION - Gene therapy. No supporting data given.

USE - (I) is useful for detecting in a test sample, the presence of an antagonist or agonist of **zsig63** protein activity. The method comprises transfecting a **zsig63**-responsive cell with a reporter gene construct that is responsive to a **zsig63**-stimulated cellular pathway, adding the **zsig63** polypeptide to the cell, in the presence and absence of the test sample, comparing the levels of response to the **zsig63** polypeptide in the presence and absence of the test sample, by a biological or biochemical assay, and determining from the comparison, the presence of the antagonist or agonist of **zsig63** activity in the test sample. (I) is also useful as an immunogen for producing an antibody to **zsig63** polypeptide, by inoculating an animal with (I), or its fragment comprising amino acids 9-204, 14-19, 16-21, 24-29, 25-30, 187-192, 24-33, 17-33, 66-73, 103-108, 190-197, 202-215, or 190-215 of (S1) and isolating the antibody from the animal (all claimed). **zsig63**-cytokine fusion proteins or antibody-cytokine fusion protein are useful for enhancing in vivo killing of target tissues. Pharmaceutical composition comprising purified **zsig63** polypeptide are useful in the treatment of conditions associated with pathological microbes, including bacterial, fungal and viral infections. High expression of **zsig63** in **salivary** gland suggests that anti-microbial polypeptides are useful for treatment of dental caries (tooth decay), periodontal disease, thrush and gastrointestinal disease. Other applications can be used in urinary tract infections, vaginal infections, prevention of infection in skin and other epithelial wounds. The polypeptides can be used to establish normal microflora and protect against pathogenic colonization and invasion. (I) is useful when pro-inflammatory activity is desired. Applications for such pro-inflammatory activity include the treatment of chronic tissue damage, particularly in areas having a limited or damaged vascular system e.g., damage in extremities associated with diabetes. Antagonists to **zsig63** polypeptides may be useful as anti-inflammatory agents. (I) is useful for the treatment of patients having incompetent immune system, such as AIDS patients or individuals that have undergone chemotherapy, radiation treatment. (I) is also useful for the treatment of lung infections associated with cystic fibrosis, for studying chemoattraction of monocytes in cell culture, for studying activity of the melanocortin family of receptors and ion flux in cell culture, and cytotoxic activity against mammalian cells. (I), its fragments, fusion proteins, or agonists are useful as cell culture reagents in in vitro studies of exogenous microorganism infection, such as bacterial, viral or fungal infection and also in in vivo animal models of infection. (I), its agonists or antagonists are useful for aiding digestion. **zsig63** is also useful to identify cells, tissues or cell lines which respond to a **zsig63**-stimulated pathway, to identify and isolate receptors for **zsig63** and in diagnostic applications. The diagnostic methods are useful in genetic linkage analysis, to detect a genetic abnormality or aberration in a patient. (V) is useful for detecting **zsig63** polypeptides.

ADMINISTRATION - Administered by topical, inhalant or parenteral, particularly intravenous or subcutaneous route. Dosage not specified.

EXAMPLE - Scanning of a translated DNA database resulted in identification of an expressed sequence tag (EST) sequence found to be a novel member of the adhesion family and designated **zsig63**. Confirmation of the EST sequence was made by sequence analyses of 25 the cDNA from which the EST originated. This cDNA clone was obtained and sequenced using the following primers ZC6768 (gcaattaaccctcactaaaggggaac, ZC694 (taatacgactcactataggg), ZC7231(ttttttttttttttttttttttttttttv) and ZC7764a (tttttttttttttttttttttttta). The insert was about 1 kb and was full-length. **zsig63** was mapped to chromosome 4. (33 pages)



ACCESSION NUMBER: 2002:276476 HCAPLUS  
 DOCUMENT NUMBER: 136:305206  
 TITLE: Protein and cDNA sequences of human secretory protein **ZSIG89**  
 INVENTOR(S): Adler, David A.; Sheppard, Paul O.; Nelson, Andrew J.  
 PATENT ASSIGNEE(S): USA  
 SOURCE: U.S. Pat. Appl. Publ., 32 pp.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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US 2002042095	A1	20020411	US 2000-741711	20001219

PRIORITY APPLN. INFO.: US 1999-172972P P 19991221  
 AB The present invention provides protein and cDNA sequences of novel human secretory protein **ZSIG89**. The expression of **ZSIG89** gene has been obsd. in fetal liver, fetal skin, spinal cord, trachea, lung tumor, rectal tumor, and genomic. Faint signals were also seen in a human prostate epithelium cell line that had been transformed with human papillomavirus, adrenal gland, prostate smooth muscle cell line, CD3+, fetal brain, pituitary, **salivary** gland, testis, and HepG2 (pancreas and liver library). The proteins include binding proteins and fusion proteins operably linked to a second polypeptide. The invention further provides therapeutic and diagnostic methods utilizing the polynucleotides, polypeptides, and antagonists of the polypeptides.

L6 ANSWER 5 OF 8 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN  
 DUPLICATE 1  
 ACCESSION NUMBER: 2002:143438 BIOSIS  
 DOCUMENT NUMBER: PREV200200143438  
 TITLE: Secreted **salivary ZSIG63** Polypeptide.  
 AUTHOR(S): Adler, David A. [Inventor, Reprint author]; Sheppard, Paul O. [Inventor]  
 CORPORATE SOURCE: Bainbridge Island, WA, USA  
 ASSIGNEE: ZymoGenetics, Inc.  
 PATENT INFORMATION: US 6331413 December 18, 2001  
 SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Dec. 18, 2001) Vol. 1253, No. 3.  
<http://www.uspto.gov/web/menu/patdata.html>. e-file.  
 CODEN: OGUPE7. ISSN: 0098-1133.  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 ENTRY DATE: Entered STN: 14 Feb 2002  
 Last Updated on STN: 26 Feb 2002

AB The present invention relates to polynucleotide and polypeptide molecules for **zsig63**, a novel secreted **salivary** protein. The polypeptides, and polynucleotides encoding them, may exhibit anti-microbial activity and may be used in the study or treatment of microbial infections. The polynucleotides encoding **zsig63**, are located on chromosome 4, and can be used to identify a region of the genome associated with human disease states. The present invention also includes antibodies to the **zsig63** polypeptides.

L6 ANSWER 6 OF 8 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN  
 DUPLICATE 2  
 ACCESSION NUMBER: 2000:349986 BIOSIS  
 DOCUMENT NUMBER: PREV200000349986  
 TITLE: Secreted **salivary zsig32** polypeptides.  
 AUTHOR(S): Sheppard, Paul O. [Inventor, Reprint author]  
 CORPORATE SOURCE: Redmond, WA, USA  
 ASSIGNEE: ZymoGenetics, Inc.

PATENT INFORMATION: US 6022847 February 08, 2000  
SOURCE: Official Gazette of the United States Patent and Trademark  
Office Patents, (Feb. 8, 2000) Vol. 1231, No. 2. e-file.  
CODEN: OGUPE7. ISSN: 0098-1133.  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
ENTRY DATE: Entered STN: 16 Aug 2000  
Last Updated on STN: 7 Jan 2002

AB The present invention relates to polynucleotide and polypeptide molecules for secreted **salivary zsig32** polypeptides. The polypeptides, and polynucleotides encoding them modulate adhesion or modulate or indicate **salivary** gland function. The present invention also includes antibodies and binding proteins for the **zsig32** polypeptides.

L6 ANSWER 7 OF 8 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN  
ACCESSION NUMBER: 2000:359345 BIOSIS  
DOCUMENT NUMBER: PREV200000359345  
TITLE: Secreted **salivary zsig32** polypeptides.  
AUTHOR(S): Sheppard, Paul O. [Inventor]  
CORPORATE SOURCE: ASSIGNEE: ZymoGenetics, Inc.  
PATENT INFORMATION: US 6025197 February 15, 2000  
SOURCE: Official Gazette of the United States Patent and Trademark  
Office Patents, (Feb. 15, 2000) Vol. 1231, No. 3. e-file.  
CODEN: OGUPE7. ISSN: 0098-1133.  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
ENTRY DATE: Entered STN: 23 Aug 2000  
Last Updated on STN: 8 Jan 2002

AB The present invention relates to polynucleotide and polypeptide molecules for secreted **salivary zsig32** polypeptides. The polypeptides, and polynucleotides encoding them modulate adhesion or modulate or indicate **salivary** gland function. The present invention also includes antibodies and binding proteins for the **zsig32** polypeptides.

L6 ANSWER 8 OF 8 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN  
ACCESSION NUMBER: 1998-11207 BIOTECHDS  
TITLE: Recombinant **zsig-32** protein involved in  
**salivary** gland and mucous associated functions;  
used in the drug screening, diagnosis and treatment of a  
range of lung, **salivary** gland, etc. disorder  
AUTHOR: Sheppard P O  
PATENT ASSIGNEE: Zymogenetics  
LOCATION: Seattle, WA, USA.  
PATENT INFO: WO 9841628 24 Sep 1998  
APPLICATION INFO: WO 1998-US5255 18 Mar 1998  
PRIORITY INFO: US 1997-41263 19 Mar 1997  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 1998-531567 [45]

AB A recombinant and isolated protein (I), designated **zsig-32**, of specified sequence is claimed along with its encoding DNA sequence (II). Also claimed are: an expression vector comprising a transcription promoter, (II) and a transcription terminator operably linked; a host cell containing an expression vector comprising (II), which expresses (I); antibody or binding protein specific for (I); a DNA probe or DNA primer composed of (II) or a complementary sequence; and a DNA construct encoding a fusion protein comprising a secretory sequence operably linked to a second protein. (I) is involved in **salivary** gland and mucous associated functions. The products can be used in the treatment, drug screening and diagnosis of digestive functions, wound healing dysfunction, inadequate saliva production, **salivary** gland cancer, pneumocystis carinii, emphysema, chronic bronchitis, cystic

fibrosis, adult respiratory distress syndrome, lung disease, tumor metastasis, xerostoma, dental caries, osteomyelitis, oral candidiasis, chronic inflammation, mumps, prostate cancer or migraine. The products can also be used as antibiotics, fungicides and virucides. (119pp)

=> d his

(FILE 'HOME' ENTERED AT 11:45:12 ON 30 JAN 2004)

FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS, LIFESCI' ENTERED AT 11:45:38 ON 30 JAN 2004

L1 6 S "ZSIG63"  
L2 4 DUP REM L1 (2 DUPLICATES REMOVED)  
L3 146427 S SALIVARY  
L4 150 S ZSIG###  
L5 12 S L3 AND L4  
L6 8 DUP REM L5 (4 DUPLICATES REMOVED)

=> s clon? or express? or recombinant

5 FILES SEARCHED...

L7 6346882 CLON? OR EXPRESS? OR RECOMBINANT

=> s l4 and l7

L8 126 L4 AND L7

=> s human and l8

L9 100 HUMAN AND L8

=> s cancer and l9

L10 23 CANCER AND L9

=> s transcription(a) activatioin or anti(w)microbial

<-----User Break----->

SEARCH ENDED BY USER

SEARCH ENDED BY USER

=> s transcription(a) activatioin or anti(w)microbial

<-----User Break----->

SEARCH ENDED BY USER

COMMAND INTERRUPTED

SEARCH ENDED BY USER

If this message appears repeatedly, please notify the Help Desk.  
Enter "HELP STN" for information on contacting the nearest STN Help  
Desk by telephone or via SEND in the STNMAIL file.

=> s transcription(a) activation or anti(w)microbial

L11 23517 TRANSCRIPTION(A) ACTIVATION OR ANTI(W) MICROBIAL

=> s l9 and l11

L12 4 L9 AND L11

=> s l11 or l12

L13 23517 L11 OR L12

=> s l12 or l10

L14 26 L12 OR L10

=> dup rem l14

PROCESSING COMPLETED FOR L14

L15 21 DUP REM L14 (5 DUPLICATES REMOVED)

=> d 1-21 ibib ab

L15 ANSWER 1 OF 21 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN  
DUPLICATE 1

ACCESSION NUMBER: 2002:400664 BIOSIS

DOCUMENT NUMBER: PREV200200400664

TITLE: Nucleic acid which encodes the tumor marker **ZSIG62**

AUTHOR(S): Sheppard, Paul O. [Inventor, Reprint author]; Novak, Julia E. [Inventor]; Raymond, Fenella [Inventor]

CORPORATE SOURCE: Granite Falls, WA, USA  
ASSIGNEE: ZymoGenetics, Inc.

PATENT INFORMATION: US 6403783 June 11, 2002

SOURCE: Official Gazette of the United States Patent and Trademark  
Office Patents, (June 11, 2002) Vol. 1259, No. 2.  
<http://www.uspto.gov/web/menu/patdata.html>. e-file.  
CODEN: OGUPE7. ISSN: 0098-1133.

DOCUMENT TYPE: Patent

LANGUAGE: English

ENTRY DATE: Entered STN: 24 Jul 2002

Last Updated on STN: 24 Jul 2002

AB Studies indicate that mutations in tumor suppressor genes occur early in the process of carcinogenesis, and that these mutations are correlated with a subsequent development of **cancer**. The detection of such alterations would provide useful molecular markers for diagnosis, surveillance, early tumor identification and intervention, and prognosis. A novel **human** gene, designated as "**Zsig62**," resides within a region of chromosome 16q that is associated with prostate and breast **cancer**, and that appears to contain tumor suppressor genes. Like a tumor suppressor gene, the **Zsig62** gene is **expressed** in particular normal tissues, but not in tumors derived from those tissues.

L15 ANSWER 2 OF 21 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN

ACCESSION NUMBER: 2002-09249 BIOTECHDS

TITLE: New polypeptides which include cytokines, growth factors and secreted proteins, useful for modulating immune reaction and inflammation and preventing or treating pancreatic disorders, diabetes and degenerative diseases;

**recombinant** fusion protein production and purification by affinity chromatography, useful for antisense gene therapy, diagnosis, transgenic animal, feedstuff, antibody production, mapping and drugdesign

AUTHOR: SHEPPARD P O; PRESNELL S R; TAFT D W

PATENT ASSIGNEE: ZYMOGENETICS INC

PATENT INFO: WO 2002002626 10 Jan 2002

APPLICATION INFO: WO 2000-US20847 30 Jun 2000

PRIORITY INFO: US 2000-215446 30 Jun 2000

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2002-154728 [20]

AB DERWENT ABSTRACT:

NOVELTY - An isolated polypeptide (I) comprising residues 23-150 of the Zcyto27 polypeptide (a member of a cytokine protein family) having a sequence of 150 amino acids, residues 19-117 of the secreted protein **Zsig96** of 117 amino acids, or residues 20-185 of the growth factor Ztth1 of 185 amino acids fully defined in the specification, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) an isolated polynucleotide (II) comprising a nucleotide sequence encoding (I); (2) an **expression** vector (III) comprising operably linked elements, a transcription promoter, a DNA segment having (II) and a transcription terminator; (3) a cultured cell (IV) comprising (III); (4) producing (I); (5) a polypeptide produced by

the above method; (6) an isolated polynucleotide encoding Zcyto27, **Zsig96** or Ztth1 and comprising a nucleotide sequence of 453, 354 or 558 base pairs (bp), respectively fully defined in the specification; and (7) an antibody (V) that specifically binds to (I).

WIDER DISCLOSURE - Also disclosed are: (1) an isolated polypeptide comprising 15 contiguous amino acid residues of Zcyto27, **Zsig96** or Ztth1 polypeptide; (2) a polynucleotide encoding a fusion protein comprising a secretory peptide of Zcyto27, **Zsig96** or Ztth1 polypeptide operably linked to a second polypeptide; (3) antisense polynucleotides that are complementary to a segment of (II); (4) a computer-readable medium encoded with a data structure; (5) reagents which include polynucleotide probes and primers for use in diagnostic and therapeutic applications; and (6) kit comprising (I), (II) or (V).

BIOTECHNOLOGY - Preparation: (I) is produced by culturing (IV) under conditions, where the sequence of nucleotides is **expressed**, and recovering the **expressed** polypeptide (claimed). Preferred Polypeptide: (I) further comprises residues 1-150, 1-117 or 1-185 of Zcyto27, **Zsig96** or Ztth1 polypeptide, respectively.

ACTIVITY - Antiinflammatory; Antiulcer; Antiinfertility; Antidiabetic; Cytostatic; Immunomodulatory.

MECHANISM OF ACTION - Gene therapy; Regulator of cellular differentiation. No supporting data is given.

USE - Zcyto27 is useful in modulating immune reaction and inflammation in kidney, liver, fetal liver, prostate, spleen, testis, thymus, lymph node and bone marrow. Molecules of **Zsig69** are useful in modulation of nutrient uptake, cell growth, differentiation and proliferation, hormones, secretion of digestive enzymes and/or secretion of enzymes and/or hormones in the pancreas, and to modulate ligand-receptor binding, inhibition or proliferation of neurons and myocytes in stomach, and to treat or prevent development of pathological conditions in stomach, brain, pituitary, hypothalamus, hippocampus, duodenum, jejunum, small intestine and pancreas. **Zsig69** polypeptides, nucleic acid molecules and antibodies are useful for diagnosis, treatment or prevention of disorders associated with for e.g. gastric reflux, gastroparesis, modulation of secretion of pituitary hormone, including growth hormone and/or growth hormone stimulating hormone, Crohn's disease, metabolic wasting, gastric ulcers, weight management, fertility, diseases of the developing reproductive system, pancreatitis, diabetes and degenerative diseases. They are also useful for treatment and prevention of pancreatic disorders associated with pathological regulation of expansion of neuroendocrine and exocrine cells in the pancreas, such as insulin-dependent diabetes mellitus (IDDM), pancreatic **cancer**, pathological regulation of blood glucose levels, insulin **expression**, insulin resistance or digestive function. (I) is useful for identifying agonists and antagonists of the polypeptide, for drug design, and as animal feed supplement and cell culture components. (I) is useful in detecting circulating autoantibodies, which are indicative of autoimmune disorders. (II) is useful for radiation hybrid mapping for constructing high-resolution contiguous maps of mammalian chromosomes and for creating transgenic animals which serve as models for **human** diseases. (I) and (II) are useful as educational tools, as laboratory practicum kits for courses related to genetics and molecular biology, protein chemistry and antibody production and analysis. The polypeptides can be used educationally as an aid to teach preparation of antibodies, identifying proteins by Western blotting and protein purification, to teach analytical skills such as mass spectrometry, circular dichroism to determine conformation, in particular the locations of disulfide bonds, X-ray crystallography to determine the three-dimensional structure in atomic detail and nuclear magnetic resonance spectroscopy to reveal the structure of proteins in solution. (V) is useful to isolate target polypeptides by affinity purification, in diagnostic assays for determining circulating or localized levels of target polypeptides, for tissue typing, cell sorting, for screening **expression** libraries, generating anti-idiotypic

antibodies, and as neutralizing antibodies or as antagonists to block protein activity in vitro and in vivo. They are also useful for studying metabolism disorders or monitoring the improvement or decline of diseases. (V) is also useful as a teaching aid to instruct students to prepare affinity chromatography columns to purify (I), **cloning** and sequencing the polynucleotides encoding an antibody and to design humanized antibodies.

ADMINISTRATION - Administered by topical, mucosal or parenteral including intravenous and subcutaneous route, at a dose of 0.01 microgram-100 mg/kg, preferably 0.1 microgram-1 mg/kg/day.

EXAMPLE - No relevant example is given. (61 pages)

L15 ANSWER 3 OF 21 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN  
ACCESSION NUMBER: 2003-14671 BIOTECHDS

TITLE: New **Zsig86** polypeptides and nucleic acid molecules useful for treating disorder associated with gonadal development, fertility, male sexual dysfunction, impotency, prostate/testicular/colon **cancer**, gastrointestinal mobility;

**recombinant** protein production, its encoding gene and antibody useful for gene therapy

AUTHOR: SHEPPARD P O; VU T Q; FELDHAUS A L; HALDEMAN B A

PATENT ASSIGNEE: SHEPPARD P O; VU T Q; FELDHAUS A L; HALDEMAN B A

PATENT INFO: US 2002192777 19 Dec 2002

APPLICATION INFO: US 2001-639 1 Nov 2001

PRIORITY INFO: US 2001-639 1 Nov 2001; US 2000-245070 1 Nov 2000

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2003-352712 [33]

AB DERWENT ABSTRACT:

NOVELTY - An isolated polypeptide comprising a sequence of 159 amino acids from residue 25-159, or 117 amino acids from residue 25-117, fully defined in the specification, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following: (1) an isolated polynucleotide that encodes the polypeptide; (2) an isolated nucleic acid molecule comprising a sequence of 477 or 351 bp, fully defined in the specification; a sequence encoding the polypeptide sequences cited above; or a nucleic acid molecule that remains hybridized following stringent wash conditions to a nucleic acid molecule consisting of nucleotides 178-582 of a sequence of 669 bp, or of nucleotides 178-456 of a sequence of 552 bp, fully defined in the specification or its complement; (3) a vector comprising the isolated nucleic acid molecule; (4) an **expression** vector comprising the nucleic acid molecule, a transcription promoter and a transcription terminator, where the promoter is operably linked with the nucleic acid molecule that is operably linked with the transcription terminator; (5) a **recombinant** host cell comprising the **expression** vector, where the host cell can be bacterium, yeast cell, fungal cell, insect cell, avian cell, mammalian cell or plant cell; (6) using the **expression** vector in producing protein by culturing the **recombinant** host cell comprising the **expression** vector that produce the protein; and (7) an antibody or antibody fragment that specifically binds to the polypeptide.

WIDER DISCLOSURE - Also disclosed includes a method for detecting the presence of **Zsig86** gene **expression** in a biological sample.

BIOTECHNOLOGY - Preparation: The Preferred Polypeptide: The polypeptide comprises at least 90% sequence identity to any of the sequences cited above. Preferred Nucleic Acid: The nucleic acid molecule encodes amino acid sequences, where any difference between these sequences is due to a conservative amino acid substitution. Preparation (Claimed): The protein was produced using standard **recombinant** procedures and was isolated from the cultured **recombinant** host cells. Preferred Antibody: The antibody can be polyclonal antibody,

murine monoclonal antibody, humanized antibody derived from the murine monoclonal antibody, or **human** monoclonal antibody.

ACTIVITY - Cytostatic; Antiinfertility; Gastrointestinal. No biological data given.

MECHANISM OF ACTION - Gene therapy.

USE - The polypeptides, nucleic acid molecules and antibodies are useful for treating disorders associated with gonadal development, pubertal changes, fertility, neuralgia associated with reproductive phenomena, male sexual dysfunction, impotency, prostate **cancer**, testicular **cancer**, colon **cancer**, gastrointestinal mobility and dysfunction. The polypeptides are useful for maintaining cellular metabolism and function. The nucleic acid molecules are useful for detecting the **expression** of a **Zsig86** gene in a biological sample. The **expression** vector is useful for producing a protein (all claimed).

ADMINISTRATION - Administration can be intravenous, intraarterial, intraperitoneal, intramuscular, subcutaneous, intrapleural, intrathecal, intranasal or by perfusion through a direct catheter or by direct intralesional injection.

EXAMPLE - PCR amplification was used for **cloning** the cDNA and the DNA fragment was purified using Gel Extraction Kit and subcloned into pCR-4-TOPO using TOPO TA **cloning** Kit for sequencing. The polynucleotide sequence of the insert corresponding to the cDNA **clone** was sequenced resulting in a sequence of 669 bp, fully defined in the specification. The deduced amino acid sequence of the insert was determined to be full-length comprising a sequence of 159 amino acids, fully defined in the specification. (46 pages)

L15 ANSWER 4 OF 21 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN  
ACCESSION NUMBER: 2003-13622 BIOTECHDS

TITLE: New pancreatic and ovarian **zsig58** polypeptides  
useful for diagnosing or treating disorders associated with  
gonadal development, pregnancy, pubertal changes, menopause,  
ovarian **cancer**, fertility, and ovarian or  
pancreatic function;  
involving vector-mediated **recombinant** protein  
gene transfer and **expression** in host cell for  
use in gene therapy

AUTHOR: SHEPPARD P O; CHANDRASEKHER Y A

PATENT ASSIGNEE: ZYMOGENETICS INC

PATENT INFO: US 2002182677 5 Dec 2002

APPLICATION INFO: US 2002-86135 26 Feb 2002

PRIORITY INFO: US 2002-86135 26 Feb 2002; US 1998-95199 3 Aug 1998

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2003-328618 [31]

AB DERWENT ABSTRACT:

NOVELTY - An isolated pancreatic and ovarian **zsig58** polypeptide comprising a sequence of amino acid residues that is at least 90% identical to a sequence having 402 amino acids (S1) given in the specification from amino acid numbers 141 (Cys) to 402 (Lys), 26 (Thr) to 402 (Lys), or 1 (Met) to 402 (Lys), is new.

DETAILED DESCRIPTION - An isolated pancreatic and ovarian **zsig58** polypeptide comprising a sequence of amino acid residues that is at least 90% identical to a sequence having 402 amino acids (S1) given in the specification from amino acid numbers 141 (Cys) to 402 (Lys), 26 (Thr) to 402 (Lys), or 1 (Met) to 402 (Lys), is new. The amino acid percent identity is determined using a FASTA program with: (i) ktup = 1; (ii) gap opening penalty = 10; (iii) gap extension penalty = 1; and (iv) substitution matrix = BLOSUM62 Other parameters are set as default.

INDEPENDENT CLAIMS are included for: (1) an isolated polynucleotide encoding the **zsig58** polypeptide; (2) an **expression** vector comprising the following operably linked elements: (a) a transcription promoter; (b) a DNA segment encoding the above

**zsig58** polypeptide comprising S1 from amino acid numbers 26 (Thr) to 402 (Lys); and (c) a transcription terminator; (3) a cultured cell into which has been introduced the **expression** vector cited above, and which **expresses** a polypeptide encoded by the DNA segment; (4) a DNA construct encoding a fusion protein, comprising a first DNA segment encoding a polypeptide having S1, and at least one other DNA segment encoding an additional segment, where the first and other DNA segments are connected in-frame and encode the fusion protein; (5) a fusion protein produced by a method comprising culturing the above host cell and recovering the protein encoded by the DNA segment; (6) a method of producing a **zsig58** polypeptide, comprising culturing the cell cited above and isolating the **zsig58** polypeptide produced by the cell; (7) a method of detecting, in a test sample, the presence of a modulator of **zsig58** protein activity, comprising: (a) transfecting a **zsig58**-responsive cell with a reporter gene construct that is responsive to **zsig58**-stimulated cellular pathway; (b) producing a **zsig58** polypeptide by method (6); (c) adding the polypeptide to the cell, in the presence and absence of a test sample; (d) comparing level of response to the **zsig58** polypeptide, in the presence and absence of the test sample, by a biological or biochemical assay; and (e) determining from the comparison, the presence of the modulator of **zsig58** activity in the test sample; (8) a method of producing an antibody to **zsig58** polypeptide, comprising: (a) inoculating an animal with a polypeptide selected from: (a) a polypeptide consisting of 9-402 amino acids, which is identical to a contiguous sequence of S1 from amino acids 26 (Thr) to 402 (Lys); (b) a polypeptide comprising S1 from residues 26 (Thr) to 140 (Ser); and (c) the polypeptide comprising 90% sequence identity to S1 (where the polypeptide elicits an immune response in the animal); and (b) isolating the antibody from the animal; and (9) an antibody produced by method (8) and which binds to the **zsig58** polypeptide cited above.

**WIDER DISCLOSURE** - Also disclosed are: (a) a method of studying insulin; and (b) a method of studying mammalian cellular metabolism.

**BIOTECHNOLOGY** - Preferred Polypeptide: The polypeptide further contains motifs 1-7 spaced apart from N-terminus to C-terminus in the configuration: (i) M1-(46)-M2-(37-41)-M3; or (ii) M4-(48-52)-M5-(49)-M1-(1)-M6-(39)-M2-(37-41)-M3-(4)-M7. The polypeptide comprises S1. Preferred Polynucleotide: The polynucleotide comprises a sequence of 2479 bp (S2) given in the specification, from nucleotides 505-1290, 160-1290 or 85-1290. The polynucleotide also comprises nucleotides 1-1206 of a sequence having 1206 bp (S3) given in the specification. Preferred **Expression Vector**: The vector further comprises a secretory signal sequence operably linked to the DNA segment. Preferred Antibody: The antibody is a monoclonal antibody. Preparation: The polypeptide was prepared using standard isolation techniques.

**ACTIVITY** - Gynecological; Osteopathic; Cytostatic; Ophthalmological; Antidiabetic; Analgesic; Vulnerary. No biological data given.

**MECHANISM OF ACTION** - Gene therapy.

**USE** - The polypeptide, nucleic acid and/or antibodies are useful in diagnosing or treating disorders associated with gonadal development, pregnancy, pubertal changes, menopause, ovarian **cancer**, fertility, ovarian function, polycystic ovarian syndrome, pancreas, diabetes, eye disease, pituitary function, osteoporosis, and other bone diseases. The **zsig58** polypeptide may also be used in promoting wound healing, in **anti-microbial** applications, as cell culture reagent in in vitro studies of exogenous microorganism infection (e.g. bacterial, viral or fungal infection), as analgesic (e.g. bone pain), in identifying cells, tissues or cell lines that respond to a **zsig58**-stimulated pathway, in identifying agonists and antagonists of its activity, and in preparing antibodies. The antibody may be used for tagging cells that **express zsig58**, for isolating **zsig58**, and for other diagnostic and therapeutic applications. The polynucleotide is also useful in identifying a region



of the genome associated with **human** disease states.

ADMINISTRATION - Administration is by parenteral means (e.g. intravenous or subcutaneous). No dosage detail given.

EXAMPLE - No relevant example given. (49 pages)

L15 ANSWER 5 OF 21 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN

ACCESSION NUMBER: 2003-13605 BIOTECHDS

TITLE: Novel isolated **zsig63** polypeptide, member of the adhesin family, useful for treating dental carries, periodontal disease, thrush, gastrointestinal disease, urinary tract infections, vaginal infections, skin infections

vector-mediated gene transfer and **expression** in host cell for **recombinant** protein production for use in disease diagnosis and gene therapy

AUTHOR: ADLER D A; SHEPPARD P O

PATENT ASSIGNEE: ADLER D A; SHEPPARD P O

PATENT INFO: US 2002173027 21 Nov 2002

APPLICATION INFO: US 2001-922469 3 Aug 2001

PRIORITY INFO: US 2001-922469 3 Aug 2001; US 1999-124820 17 Mar 1999

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2003-328428 [31]

AB DERWENT ABSTRACT:

NOVELTY - An isolated **zsig63** polypeptide (I) comprising at least 90 % identity to an amino acid sequence which comprises amino acids 16(Arg)-37(Ser) (domain 1 of **zsig63**), 38(Leu)-126(Ala) (domain 2), 127(Pro)-219(Gln) (domain 3), 16(Arg)-219(Gln) (mature **zsig63** polypeptide) or 1(Met)-219(Gln) of a 219 amino acid sequence (S1), given in the specification, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for: (1) an isolated polynucleotide (II) encoding (I); (2) an **expression** vector (III) comprising the following operably linked elements, a transcription promoter, DNA segment encoding a **zsig63** polypeptide comprising an amino acid sequence that is at least 90 % identical to amino acids 16(Arg)-219(Gln) of (S1), and a transcription terminator; (3) a cultured cell (IV) into which has been introduced (III), where the cell **expresses** a polypeptide encoded by the DNA segment; (4) a DNA construct (V) encoding a fusion protein, comprising a first DNA segment encoding a polypeptide chosen from amino acid sequence (S1) from residues 1(Met)-15(Ala), 16(Arg)-37(Ser), 38(Leu)-126(Ala), 127(Pro)-219(Gln), 16(Arg)-219(Gln), and at least one other DNA segment encoding an additional polypeptide, where the first and other DNA segments are connected in-frame, and encode the fusion protein; (5) a fusion protein (VI) produced by culturing a host cell into which has been introduced a vector comprising operably linked transcriptional promoter, (V), and transcriptional terminator, and recovering the protein encoded by the DNA segment; (6) producing (I); (7) detecting in a test sample, the presence of agonist of **zsig63** protein activity, comprising: (a) transfecting a **zsig63**-responsive cell with a reporter gene construct that is responsive to **zsig63**-stimulated cellular pathway, adding a test sample; and (b) comparing levels of response in the presence and absence of the test sample, by a biological or biochemical assay, and determining from the comparison, the presence of the agonist of **zsig63** activity in the sample; (8) producing an antibody to **zsig63** polypeptide, which involves inoculating an animal with a polypeptide consisting of 9-204 amino acids, which consists of a contiguous sequence of amino acids in (S1) from amino acids 16(Ala)-219(Gln), (I), and a polypeptide comprising amino acids 16(Arg)-37(Ser), 38(Leu)-126(Ala), 127(Pro)-219(Gln), 16(Arg)-219(Gln), 1(Met)-219(Gln), 14(Phe)-19(Arg), 16(Arg)-21(Phe), 24(Gly)-29(Asp), 25(Glu)-30(Asp), 187(Glu)-192(Glu), 24(Gly)-33(Pro), 17(Lys)-33(Pro), 66(Thr)-73(Pro), 103(Pro)-108(Gly), 190(Ala)-197(Glu), 202(Lys)-215(Gly) or 190(Ala)-215(Glu) of (S1), where the polypeptide elicits an immune

response in the animal to produce the antibody, and isolating the antibody from the animal; (9) an antibody (VII) produced by the method of (8), which binds to (I); and (10) an antibody (VIII) that binds to (I).

WIDER DISCLOSURE - (1) counterpart polypeptides and polynucleotides of **zsig63**; (2) allelic and splice variants of (S1) and (S2); (3) functional fragments of (I) and the polynucleotides encoding the fragments; (4) identifying agonist and antagonist of **zsig63** polypeptide using a microphysiometer; and (5) mice engineered to **express zsig63** gene referred to as transgenic mice, and mice that exhibit complete absence of **zsig63** gene function referred to as knockout mice.

BIOTECHNOLOGY - Preparation: (I) is produced by culturing (IV) and isolating the polypeptide produced by the cell (claimed). Preferred Polynucleotide: (I), preferably comprises an amino acid sequence which comprises amino acid residues 16(Arg)-37(Ser), 38(Leu)-126(Ala), 127(Pro)-219(Gln), 16(Arg)-219(Gln) or 1(Met)-219(Gln) of (S1). (II) nucleotides 173-784 or 128-784 of a 1008 nucleotide sequence (S2), given in the specification, or a polynucleotide sequence complementary to the sequence. Optionally, (II) comprises nucleotides 1-657 of a fully defined degenerate sequence of (S1) which has 657 nucleotides, given in the specification. Preferred Vector: (III) further comprises a secretory signal sequence operably linked to the DNA segment. Preferred Antibody: (VII) is a monoclonal antibody.

ACTIVITY - Antimicrobial; Antibacterial; Vulnerary. No biological data is given.

MECHANISM OF ACTION - Gene therapy.

USE - (I) is useful for detecting in a test sample, the presence of antagonist of **zsig63** protein activity, which involves transfecting a **zsig63**-responsive cell with a reporter gene construct that is responsive to **zsig63**-stimulated cellular pathway, and producing (I) by **recombinant** techniques, and adding (I) to the cell in the presence and absence of the test sample, and comparing level of response to the polypeptide in the presence and absence of the test sample, by a biological or biochemical assay, and determining from the comparison, the presence of the antagonist of **zsig63** activity in the sample. (IV) is useful for producing (I) by standard **recombinant** methods. (All claimed.) (I) comprises 16 full evenly-spaced coil-like repeats in domain 2. The coil-like repeats are useful for identifying new family members. (I) and (II) are useful for identifying and isolating receptors that bind to **zsig63** polypeptide. (I) has antimicrobial activity and since exhibits high **expression** in salivary gland, can be used for treating dental carries, periodontal disease, thrush, and gastrointestinal disease, urinary tract infections, vaginal infections, skin infections and other epithelial wounds. The polypeptides can be used to establish normal microflora and protect against pathogenic colonization and invasion. (I) can also be used for providing pro-inflammatory activity for treating chronic, tissue damage particularly in areas having limited or damaged vascular system, e.g. damage in extremities associated with diabetes. (I) is also useful for treating conditions where stimulation of immune responsiveness is desired, e.g. AIDS patient or in individuals that have undergone chemotherapy, radiation treatment, etc. (I) is also useful for treating lung infections associated with cystic fibrosis. (I) is useful for studying chemoattraction of monocytes in cell culture, studying activity of melanocortin family of receptors in cell culture, studying ion flux in cell culture, studying cytotoxic activity in mammalian cell such as tumor cells in cell culture, as cell culture reagents in in vitro studies of exogenous microorganism infection such as bacterial, viral or fungal infections, and for studying epithelial cell defensin induction in cell culture. (I) is useful as a diagnostic reagent e.g. **zsig63** polypeptide is detected in the serum or tissue biopsy of a patient, for evaluating salivary gland function or dysfunction (e.g. digestive dysfunction, wound healing dysfunction, inadequate saliva production or

composition, mucosal integrity breakdown, and failure or diminished **anti-microbial** function. Detection of **zsig63** polypeptide at relatively high levels in the trachea may indicate that such polypeptides may serve as a marker of lung dysfunction. (I) is also useful as a diagnostic reagent for conditions associated with salivary gland or lung dysfunction including salivary gland carcinoma, Pneumocystis carinii infection (particularly associated with AIDS patient), emphysema, chronic bronchitis, etc. (I) is also useful for diagnosing prostate dysfunctions such as prostate adenocarcinoma. (I) is useful for aiding digestion, and as components of defined cell culture media and may be used alone or in combination with other cytokines and hormones to replace serum that is commonly used in culture. The **zsig63** polypeptides are useful as research reagent such as for the expansion of cultured cells, and as immunogen to prepare anti-**zsig63** antibodies. (II) is useful in gene therapy applications to increase or inhibit **zsig63** activity, and for detecting abnormalities on **human** chromosome 4 associated with disease or other **human** traits. **Zsig63** polynucleotide probes can be used to detect abnormalities or genotypes associated with genes located at the 4q12-4q13 region of chromosome 4, e.g. dentinogenesis imperfecta, and dentin dysplasia type II.

ADMINISTRATION - (I) is administered by topical, inhalant, parenteral, preferably intravenous or subcutaneous delivery. No dosages is given.

EXAMPLE - Scanning of a translated DNA database resulted in identification of an **expressed** sequence tag (EST) sequence found to be a novel member of the adhesin family and designated **zsig63**. Confirmation of the EST sequence was made by sequence analyses of the cDNA from which the EST originated. This cDNA clone was obtained and sequenced. Northern blot tissue distribution of the mRNA revealed high **expression** in salivary gland, and moderate to high **expression** in thyroid. (32 pages)

L15 ANSWER 6 OF 21 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN

ACCESSION NUMBER: 2003-08077 BIOTECHDS

TITLE: New secretory protein-48 (**Zsig48**) polypeptides, useful for promoting proliferation of blood leukocytes and subsequently treating **cancer** patients whose leukocytes have been depleted by chemotherapy; vector-mediated gene transfer and **expression** in host cell for **recombinant** protein production, vaccine adjuvant and disease therapy

AUTHOR: LOK S; SHEPPARD P O; KINDSVOGEL W; BORT S J

PATENT ASSIGNEE: ZYMOGENETICS INC

PATENT INFO: US 2002132996 19 Sep 2002

APPLICATION INFO: US 2001-955807 19 Sep 2001

PRIORITY INFO: US 2001-955807 19 Sep 2001; US 1998-102679 1 Oct 1998

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2003-155903 [15]

AB DERWENT ABSTRACT:

NOVELTY - An isolated secretory protein-48 (**Zsig48**) polypeptide comprising: (a) a sequence that is 90 % identical with a sequence of 105, 79, 77, 65, 89 or 80 amino acids (designated P1 - P6, respectively) given in the specification; or (b) a sequence consisting of 20, 42, 65, 20 or 43 amino acids (designated P7 - P11, respectively), given in the specification.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) an isolated polynucleotide which encodes a polypeptide that is 90 % identical with a sequence selected from P1 - P6, or which encodes a polypeptide having a sequence selected from P7 - P11; (2) an isolated antibody that binds to a polypeptide comprising a sequence that is identical with P1 - P6; (3) an isolated anti-idiotypic antibody which binds to an epitope of an antibody of (2); and (4) promoting

proliferation of leukocytes by bringing the leukocytes in contact with a polypeptide comprising a sequence that is 90 % identical with P1 - P6.

WIDER DISCLOSURE - Also disclosed are the following: (1) an isolated nucleic acid molecule encoding a **Zsig48** polypeptide comprising a sequence of 1692 base pairs (bp) given in the specification, or 70 - 99 % identical to this sequence; (2) **expression** vectors comprising the nucleic acid; (3) **recombinant** host cells comprising and **expressing** the vectors; (4) antibodies and antibody fragments that specifically bind with **Zsig48** polypeptides; (5) detecting an alteration in a chromosome containing **Zsig48**; and (6) diagnosing an alteration in the **Zsig48** gene of an individual.

BIOTECHNOLOGY - Preparation: The **Zsig48** polypeptides may be produced by standard **recombinant** techniques.

ACTIVITY - Cytostatic; Immunostimulant. No biological data is given.

MECHANISM OF ACTION - Protein therapy; Vaccine.

USE - **Zsig48** polypeptides are useful for promoting proliferation of blood leukocytes and thus to treat **cancer** patients whose leukocytes have been depleted by chemotherapy, radiation or illness, and to treat immunosuppressed individuals as in the elderly or **human** immunodeficiency virus (HIV) infected individuals. These may also be used as a vaccine adjuvant. **Zsig48** nucleic acid molecules may be used to detect the **expression** of a **Zsig48** gene in a biological sample, as probes for in vivo diagnosis to detect and localize **Zsig48** gene **expression** in tissue samples, and to determine whether a subject's chromosome contains a mutation in the **Zsig48** gene.

ADMINISTRATION - Administration can be intravenous, intraarterial, intraperitoneal, intramuscular, subcutaneous, intrapleural, intrathecal, oral, dermal, mucosal-membrane, pulmonary, transcutaneous, by perfusion through a regional catheter, or by direct intralesional injection. Dosage is 1 pg - 10 mg/kg body weight, preferably 4 - 100 micrograms/kg per day.

EXAMPLE - The **expressed** sequence tag of a 384 base pair (bp) sequence was discovered through random sequencing of a mixed hematopoietic cDNA library, and the full length **clone** isolated and sequenced, resulting in a sequence of 1692 bp and 105 amino acids. Analysis of the 1.6 kb insert in pSLzsig48 revealed the presence of an EcoRI adapter sequence used for cDNA synthesis at the 5' end of the insert. At the 3' end of the insert was an XhoI site, which lacked the flanking sequence that was present on the oligonucleotide primer. This suggested that the pSLzsig48 insert might be derived from a genomic contaminant that co-purified with the cDNA preparation. (45 pages)

L15 ANSWER 7 OF 21 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN

ACCESSION NUMBER: 2002-15389 BIOTECHDS

TITLE: New **human ZSIG89** polypeptides and polynucleotides, useful for treating microbial infection, **cancer**, autoimmune disorders, bone disorders, inflammation, immunodeficiencies, wound, tumor, diabetes, pneumonia, asthma, emphysema and allergy; vector-mediated gene transfer, **expression** in host cell, antisense oligonucleotide, DNA probe and DNA primer for **recombinant** protein production, drug screening and gene therapy

AUTHOR: ADLER D A; SHEPPARD P O; NELSON A J

PATENT ASSIGNEE: ADLER D A; SHEPPARD P O; NELSON A J

PATENT INFO: US 2002042095 11 Apr 2002

APPLICATION INFO: US 1999-741711 21 Dec 1999

PRIORITY INFO: US 2000-741711 19 Dec 2000

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2002-315124 [35]

AB DERWENT ABSTRACT:

NOVELTY - An isolated polypeptide (I) comprising residues 27-325 of a fully defined sequence (S1) of 325 amino acids as given in the specification, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) an isolated polynucleotide (II) encoding (I); (2) an **expression** vector (III) comprising the following operative linked elements: (a) a transcription promoter; (b) a DNA segment, which is (II); and (c) a transcription terminator; (3) a cultured cell (IV) into which has been introduced (III), where the cell **expresses** (I); (4) producing (I) comprising culturing (IV) and recovering (I); (5) an epitope-bearing portion (V) of (I), where the epitope bearing region comprises 30 contiguous amino acids; (6) producing (M1) an antibody (VI) comprising: (a) inoculating an animal with a polypeptide comprising residues 1-26, 27-325 or 1-325 of S1, where the polypeptide elicits an immune response in the animal to produce the antibody and isolating the antibody; or (b) inoculating an animal with (V), where the polypeptide elicits an immune response in the animal to produce the antibody and isolating the antibody, where the antibody binds to the epitope-bearing portion; or (7) an antibody produced by M1; (8) a monoclonal antibody that binds to (I); and (9) detecting the presence of **ZSIG89** gene **expression** in a genetic sample comprising: (a) incubating the genetic sample with a polynucleotide probe or primer which comprises a portion of (II) and hybridizes to a complementary polynucleotide sequence, producing a reaction product and detecting the formation of hybrids of the probe or primer and the genetic sample in the reaction product, where the presence of the hybrids indicates the presence of **ZSIG89** gene **expression**; or (b) contacting the biological sample with (VI) or its fragment and detecting the presence of bound (VI) or its fragment, where the presence of the bound (VI) or its fragment indicates the presence of **ZSIG89** gene **expression**.

WIDER DISCLOSURE - Also disclosed as new are: (1) isolated and purified **ZSIG89** polynucleotide probes; (2) fusion proteins comprising **ZSIG89** proteins; and (3) (ant)agonists of **ZSIG89**.

BIOTECHNOLOGY - Preparation: (I) can be produced according to standard **recombinant** techniques. Preferred Polypeptide: (I) comprises residues 1-325 of S1 or an amino acid sequence at least 90% identical to S1. Any difference between the isolated polypeptide and S1 is due to conservative amino acid substitution. Preferred Vector: In (III), the DNA segment contains an affinity tag. Preferred Method: Producing (I) further comprises isolating **ZSIG89** protein from the cultured cell. Preferred Antibody: (VI) specifically binds residues 1-325 of S1.

ACTIVITY - Antibacterial; Antifungal; Antiviral; Cytostatic; Immunosuppressive; Immunostimulant; Osteopathic; Antiinflammatory; Vulnerary; Antidiabetic; Antiasthmatic; Antiallergic.

MECHANISM OF ACTION - Gene therapy; Antisense therapy. No supporting data is given.

USE - **ZSIG89** polypeptides, polynucleotides and antibodies and its (ant)agonists are useful for treating microbial infections (such as bacterial, yeast and viral), **cancer**, autoimmune disorders, bone disorders, inflammation, immunodeficiencies, wounds, tumors, insulin dependent diabetes mellitus, pneumonia, asthma, emphysema and allergies.

ADMINISTRATION - The proteins can be administered intravaginally, orally, rectally, parenterally (particularly intravenous or subcutaneous), intracisternally, intraperitoneally, topically, buccally or as a pulmonary or nasal inhalant. Therapeutic doses are in the range of 0.1-100 microgram/kg of patient weight per day, preferably 0.5-20 mg/kg of patient weight per day.

EXAMPLE - None given in the source material. (31 pages)

TITLE: Novel isolated **zsig45** polypeptide useful for treating or preventing disorders associated with thyroid dysfunction, inflammatory diseases, heart diseases, pancreatic disorders, atherosclerosis, restenosis, obesity; involving vector-mediated **recombinant** protein gene transfer and **expression** in host cell for use in disease prevention and therapy

AUTHOR: DEISHER T A; SHEPPARD P O

PATENT ASSIGNEE: ZYMOGENETICS INC

PATENT INFO: US 6500925 31 Dec 2002

APPLICATION INFO: US 2000-522980 10 Mar 2000

PRIORITY INFO: US 2000-522980 10 Mar 2000; US 1997-67263 3 Dec 1997

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2003-340475 [32]

AB DERWENT ABSTRACT:

NOVELTY - An isolated **zsig45** polypeptide (I) comprising or consisting of sequence of amino acid residues 47(Lys)-114 (Asp) or 1(Met)-114(Asp) of a fully defined sequence of 114 amino acids (S2), amino acid residues 1(Met)-85(Asp) of fully defined sequence of 85 amino acids (S4), or amino acid residues 1(Met)-89(Asp) of a fully defined sequence of 89 amino acids (S3), is new.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for an isolated fusion polypeptide comprising a first segment which comprises a polypeptide having a sequence of amino acid residues chosen from 1-46 or 47-114 of (S2), amino acids 1-21 of (S3) or amino acids 1-17 of (S4), and a second segment comprising an additional polypeptide where the first and second segments are connected and comprise the fusion protein.

BIOTECHNOLOGY - Preferred Polypeptide: (I) preferably comprises or consists of amino acid residues 47-114 of (S2). (I) further binds to an antibody which is raised against a polypeptide comprising sequence of amino acid residues 47-114 or 1-114 of (S2), 1-85 of (S4) or 1-89 of (S3), where the binding of the antibody to (I) is measured by a biological or biochemical assay chosen from a radio immunoassay, radioimmunoprecipitation, Western blot, or enzyme-linked immunosorbent assay. (I) has proinflammatory activity. (I) further comprises an affinity tag, radionuclide, enzyme, substrate, cofactor, inhibitor, fluorescent marker, chemiluminescent marker or magnetic particle. Preparation: (I) was prepared using standard **recombinant** techniques.

ACTIVITY - Vasotropic; Antiinflammatory; Osteopathic; Cytostatic; Vulnerary; Anti-HIV; Virucide; Antiatherosclerotic; Anorectic; Hypotensive; Antidiabetic; Antiulcer.

MECHANISM OF ACTION - Inhibitor of viral replication; Stimulates proliferation or differentiation of cardiac myocytes; Inhibits proliferation or differentiation of adipocytes; Promoter of angiogenesis. No supporting data is given.

USE - **zsig45** polypeptide is useful for treating disorders associated with thyroid dysfunction. (I) is useful for treating or preventing development of pathological conditions in diverse tissues as thyroid, heart and bone, e.g., thyroid disorders, ischemia reperfusion injury, inflammatory disorders, etc. **zsig45** polypeptide that interacts with the calcitonin receptor or exert other effects on bone, is used in therapeutic applications for which calcitonin is useful, e.g., treatment of osteoporosis, Paget's disease, hyperparathyroidism, osteomalacia, idiopathic hypercalcemia of infancy, etc. (I) is also useful for inhibiting secretion in the treatment of acute pancreatitis and gastrointestinal disorders. **zsig45** polypeptide is **expressed** in colon, and can be useful in promoting wound healing in this tissue. The polypeptide is useful in treatment of inflammatory bowel disease, diverticulitis, inflammation during and after intestinal surgery. **zsig45 expressed** in thyroid can have wound-healing or antimicrobial or antiviral actions in tissues outside of thyroid such as heart, brain, liver, kidney. **zsig45** polypeptide

exhibits antiviral activity by inhibiting viral replication by specific signaling by its receptors on a host cell (e.g., T cell). Thus **zsig45** polypeptide may be used as an antiviral therapeutic, for example, for viral leukemias (**human** T-cell lymphotropic virus (HTLV)), AIDS (HIV), or gastrointestinal infections caused by rotavirus, calicivirus, etc. (I) is useful for inhibiting chondrosarcomas, atherosclerosis, restenosis and obesity. (I) is useful in the elucidation and prevention of various thyroid diseases, inflammation, bone diseases, inflammation, menstrual problems, heart diseases, bone, colon, pituitary, and thyroid **cancers**. **zsig45** polypeptides may be used to modulate cellular metabolite reactions such as adipogenesis, gluconeogenesis, glycogenolysis, lipogenesis, glucose uptake, protein synthesis, thermogenesis, oxygen utilization; and in organ preservation for cryopreservation for surgical pretreatment to prevent injury due to ischemic and/or inflammation. **zsig45** polypeptide is useful treatment of pancreatic disorders, and in treatment of heart disease or malfunctions in myocardial contractility, or pathologies associated with genetic and other **human** disease states such as diabetes, bone disease, hematopoietic disorders, immune disorders, leukemias, hypertension, cardiac hypertrophy, other cardiac disorders and neural diseases. **zsig45** polypeptide is useful for limiting infarct size following a heart attack, aiding in recovery after heart transplantation, and promoting wound healing following angioplasty or endarterectomy to develop coronary collateral circulation, for revascularization in the eye for complications related to poor circulation such as diabetic foot ulcers, for stroke; improving cardiac function either by inducing coronary collateral development. (I) is useful for inducing remodeling of necrotic myocardial area, skeletal muscle neogenesis and/or hyperplasia, kidney regeneration and/or for treatment of systemic and pulmonary hypertension. (I) is useful as component of defined cell culture media, and in combination with other cytokines and hormones to replace serum that is commonly used in cell culture. **zsig45** polypeptide can be used to identify and isolate receptors involved in thyroid, pituitary, cardiac or other function to which **zsig45** polypeptide bind in vivo, and to identify cells, tissues or cell lines which respond to **zsig45**-stimulated pathway. Measurement of **zsig45** polypeptide can be useful in diagnosing inflammatory diseases such as melanoma, asthma, pelvic inflammatory disease, psoriasis, arthritis, reperfusion ischemia. (I) is useful for studies to isolate mesenchymal stem cells and cardiac myocyte progenitor cells, both in vivo and ex vivo.

**ADMINISTRATION** - The polypeptides are administered intravenously, intraarterially, or intraductally or may be introduced at the intended site of action.

**EXAMPLE** - Identification of **zsig45** was carried out as follows. Scanning of a translated in-house pituitary library DNA database using a signal trap as a query resulted in identification of an **expressed** sequence tag (EST) sequence found to be homologous to a **human** secretory signal sequence. Oligonucleotide primers were designed from the sequence of identified EST. The primers were used for priming internally within the EST to isolate a full-length **clone** from the **human** pituitary cDNA library. To obtain a full-length cDNA, 3' rapid amplification of cDNA ends (RACE) was employed. A 3' RACE product was generated using a **human** pituitary cDNA library as template and oligonucleotides SC694 (TAATACGACCACTATAGGG) and SC14030 (CGCAGATCAGGAAGCACCGGAAGA) as primers. The resulting DNA products were electrophoresed on a 1.5% agarose gel, and a prominent band at approximately 650 bp was seen. The DNA band was gel purified and subcloned into a PCR-blunt vector. Sequence analyses of the subclone revealed that the DNA products included the EST DNA sequence. This 650 bp insert was liberated from the vector by restriction enzyme digestion with EcoRI and was electrophoresed. The fragment was purified and then radioactively labeled with 32P-dCTP. The probe was then purified using a Nuc-Trap column. **ExpressHyb** solution was used for

prehybridization and as a hybridizing solution for colony lifts of the **human** pituitary library. Hybridization took place overnight at 65degreesC using 5x10<sup>6</sup> counts per minute (cpm)/ml of labeled probe. The colony lifts were then washed in 2X saline sodium citrate (SSC)/1% sodium dodecyl sulfate (SDS) at 65degreesC followed by a wash in 0.1X SSC/0.1% SDS at 55degreesC. Hybridizing **clones** were isolated and discovered to contain a full-length cDNA encoding **zsig45** protein. Northern blot analysis was performed and results showed highest signal intensity for thyroid. No signals at 650 bp were present in any other tissues represented by the blots. DotBlots were also performed using **Human** RNA Master Blots. Strong signal intensity was present in thyroid gland, and pituitary gland. Less intense signals were indicated in colon. (37 pages)

L15 ANSWER 9 OF 21 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN  
ACCESSION NUMBER: 2003-12728 BIOTECHDS

TITLE: New antibody which binds to **human** thyroid protein, **zsig45**, useful for treating and preventing disorders associated with thyroid dysfunction and myocardial infarction, and also inflammatory disorders;  
monoclonal antibody production for disease diagnosis, therapy and prevention

AUTHOR: DEISHER T A; SHEPPARD P O

PATENT ASSIGNEE: ZYMOGENETICS INC

PATENT INFO: US 6486304 26 Nov 2002

APPLICATION INFO: US 2000-523462 10 Mar 2000

PRIORITY INFO: US 2000-523462 10 Mar 2000; US 1997-67263 3 Dec 1997

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2003-298173 [29]

AB DERWENT ABSTRACT:

NOVELTY - An antibody (I) which binds to a **human** thyroid protein **zsig45** comprising a fully defined sequence (S1-S3) of 114, 85 or 89 amino acids, respectively, given in the specification, or a mature **zsig45** polypeptide without the signal peptide comprising amino acids 47-114 of (S1), is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) producing (M) an antibody to a polypeptide, by inoculating an animal with a polypeptide consisting of 9-67 amino acids, identical to a contiguous sequence of (S1) from amino acids 47-114, a polypeptide comprising amino acids 50-56, 61-66, 71-76, 87-92 or 95-100 of (S1), a polypeptide comprising (S2) or (S3), a polypeptide consisting of a hydrophilic peptide predicted from a hydrophobicity plot of the **zsig45** polypeptide using a Hopp/Woods hydrophilicity profile based on a sliding six-residue window, with buried G, S and T residues and exposed H, Y and W residues ignored, where the polypeptide elicits an immune response in the animal to produce the antibody, and isolating the antibody from the animal; and (2) an antibody (I) produced by (M1) which binds to **zsig45** polypeptide.

BIOTECHNOLOGY - Preferred Antibody: (I) is a monoclonal antibody.

ACTIVITY - Antithyroid; Antiinflammatory; Vasotropic; Cardiant; Vulnerary; Antiulcer; Cerebroprotective; Hypotensive. No biological data given.

MECHANISM OF ACTION - Antibody therapy; Antagonists of **zsig45**.

USE - (I) is useful for treating disorders associated with thyroid dysfunction and to treat or prevent development of pathological conditions in such diverse tissue as thyroid, heart and bone. Diseases that may be amenable to such diagnosis, treatment or prevention include thyroid disorders, ischemia reperfusion injury, and inflammatory disorders. (I) is also useful for treating disorders associated with myocardial infarction, congestive heart failure, hypertrophic cardiomyopathy and dilated cardiomyopathy. (I) is further useful for limiting infarct size following a heart attack, aiding in recovery after



heart transplantation, promoting angiogenesis and wound healing following angioplasty or endarterectomy, to develop coronary collateral circulation, for revascularization in the eye, for complications related to poor circulation such as diabetic foot ulcers, for stroke, following coronary reperfusion using pharmacologic methods, and other indications where angiogenesis is of benefit. (I) is also useful for inducing skeletal muscle neogenesis and/or hyperplasia, kidney regeneration and/or for treating systemic and pulmonary hypertension. Direct measurement of **zsig45** antibodies is useful in diagnosing inflammatory diseases such as melanoma, inflammatory bowel disease, diverticulitis, asthma, pelvic inflammatory disease, psoriasis, arthritis, reperfusion ischemia, and other inflammatory diseases. (I) is useful for tagging cells that **express zsig45**, for isolating **zsig45** by affinity purification, for diagnostic assays for determining circulating levels of **zsig45** polypeptides, for detecting or quantitating soluble **zsig45** as marker of underlying pathology of disease, in analytical methods employing FACS, for screening **expression** libraries, for generating anti-idiotypic antibodies and as neutralizing antibodies or as antagonists to block **zsig45** activity in vitro and in vivo. Antibodies can be directly or indirectly conjugated to drugs, toxins, and radionuclides and can be used for in vivo diagnostic or therapeutic applications. (I) or its fragment can be used in vitro to detect denatured **zsig45** in assays for e.g. Western Blots or other assays.

ADMINISTRATION - Administration is by parenteral, particularly intravenous or subcutaneous routes. Dosage not given.

EXAMPLE - No relevant example given. (37 pages)

L15 ANSWER 10 OF 21 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN  
ACCESSION NUMBER: 2001-12940 BIOTECHDS

TITLE: Novel secreted protein, **zsig87** polypeptides and polynucleotides for detecting **human** chromosomal abnormalities, as immunocontraceptives and for diagnosing, treating **cancer**, cardiovascular and inflammatory disease;

**recombinant** protein gene production useful in gene therapy

AUTHOR: Sheppard P O  
PATENT ASSIGNEE: Zymogenetics  
LOCATION: Seattle, WA, USA.  
PATENT INFO: WO 2001042292 14 Jun 2001  
APPLICATION INFO: WO 2000-US33539 8 Dec 2000  
PRIORITY INFO: US 1999-456641 8 Dec 1999  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 2001-381639 [40]

AB An isolated secreted protein **zsig87** is claimed. It contains a sequence of amino acid residues that is 90% identical to a sequence (S1) of 84 amino acids or amino acid residues 27-56 or 16-84 of (S1) fully defined. Also claimed are: an isolated polynucleotide (I); a DNA construct (II); an **expression** vector (III); a cultured cell (IV); a fusion protein; producing **zsig87** protein; an antibody (V); detecting genetic abnormality in a patient; and detecting **cancer** in a patient. **Zsig87** proteins are useful for producing antibodies, which are useful for detecting **cancer** in a patient. **Zsig87** is useful for identifying modulators of its activity, which are useful for treating cardiovascular disease, infertility, in vitro fertilization, birth control, treating impotence or other male reproductive dysfunctions. **Zsig87** proteins are useful for promoting wound healing. **Zsig87** proteins and its modulators are useful for treating diabetes, pancreatic **cancer** and inflammatory disease. **Zsig87** polynucleotide sequences are useful as DNA probes or DNA primers. Antibodies to **zsi87** are useful for isolating **zsig87** by affinity purification. (107pp)

L15 ANSWER 11 OF 21 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN  
ACCESSION NUMBER: 2002-08372 BIOTECHDS

TITLE: New **zsig87** polynucleotides and encoded polypeptides, useful for, e.g., studying pancreatic cell proliferation or differentiation, mammalian cellular metabolism, promoting wound healing, or treating **cancers**;  
vector-mediated **recombinant** protein gene transfer and **expression** in host cell, monoclonal antibody, agonist, antagonist, DNA probe and DNA primer for use in gene therapy

AUTHOR: SHEPPARD P O  
PATENT ASSIGNEE: SHEPPARD P O  
PATENT INFO: US 2001044134 22 Nov 2001  
APPLICATION INFO: US 1999-733523 8 Dec 1999  
PRIORITY INFO: US 2000-733523 8 Dec 2000  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 2002-105570 [14]

AB DERWENT ABSTRACT:

NOVELTY - A polypeptide comprising a sequence of amino acid residues that is at least 90% to a sequence comprising amino acids 27 (R)-56 (C) (AA1), amino acids 16 (E)-84 (P) (AA2), or amino acids 1(M)-84(P) (AA3) of a specified 84 amino acid sequence (I) (not defined in the specification), is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) an **expression** vector comprising the following operably linked elements: a transcription promoter, a DNA segment encoding AA1 comprising amino acids 16-84, and a transcription terminator; (2) a cultured cell into which has been introduced an **expression** vector of (1) and which **expresses** the polypeptide encoded by the DNA segment; (3) a DNA construct comprising a first segment encoding AA1, AA2 or AA3, and at least one other DNA segment encoding an additional polypeptide, where the DNA segments are connected in-frame and encode a fusion protein; (4) a fusion protein produced by culturing a host cell into which has been introduced a vector comprising the operably linked elements transcriptional promoter, a DNA construct of (3) and a transcriptional terminator; (5) an isolated polynucleotide encoding a polypeptide comprising a amino acid sequence that is at least 90% identical to AA1, AA2 or AA3; (6) a method of producing a polypeptide by culturing a host cell of (2) and isolating the polypeptide produced by the cell; (7) a method of producing an antibody to a polypeptide by inoculating an animal with a polypeptide selected from a polypeptide of (5), AA1, AA2, a polypeptide comprising amino acids 57-84, 39-45, 41-47, 68-73, 77-82 and 68-82 of (I), where the polypeptide elicits an immune response in the animal to produce the antibody, and isolating the antibody from the animal; (8) an antibody produced from the method of (7), or which specifically binds to the polypeptide of (5); and (9) methods for detecting a genetic abnormality or **cancer** in a patient.

WIDER DISCLOSURE - Also disclosed is a method of detecting modulators of **zsig87** protein activity.

BIOTECHNOLOGY - Preparation: The polypeptide was prepared using standard **recombinant** procedures. Preferred Polypeptide: The polypeptide is encoded by a sequence comprising nucleotides 198-287 (S1), 165-371 (S2), or 120-371 of a 456 bp sequence, (not defined in the specification), or the complement of S1 or S2. The polynucleotide may alternatively comprise a sequence of nucleotides 1-252 of defined sequence (II) (not given in the specification). The polynucleotide encodes a polypeptide that further comprises a cysteine motif spaced apart from N-terminus to C-terminus in a configuration represented by (A): C = Cysteine; G = Glycine; K/R = Lysine or Arginine; () = number of amino acid residues between the amino acids; and (9/13) =

number of amino acid residues between the amino acids is 9 or 13. Preferred Vector: The vector further comprises a secretory signal sequence operably linked to the DNA segment. Preferred Methods: Detecting genetic abnormality in a patient comprises producing a first reaction product by incubating the genetic sample with at least 14 contiguous nucleotides of (I), or a complement of (I), under conditions allowing the polynucleotide to hybridize to the complementary sequence of the polynucleotide; visualizing the first reaction product; and comparing the first reaction product to control reaction product from a patient, where the difference between the first reaction product and the control indicates genetic abnormality. Detecting a **cancer** in a patient comprises obtaining a tissue or biological sample from a patient; incubating the sample with an antibody that specifically binds to the polypeptide defined above, under conditions where the antibody binds to the complementary polypeptide in the sample; visualizing the antibody bound in the sample; and comparing the level of antibody bound in the sample from the patient, with that of a control tissue. Alternatively, the method comprises incubating the sample obtained from the patient with a labeled polynucleotide comprising at least 14 contiguous of (I) or the complement of (I); visualizing the labeled polynucleotide in the sample; and comparing the level of labeled polynucleotide to a control sample. An increase or decrease in the level of the antibody bound to the sample, or in the amount of labeled polynucleotide hybridization relative to the control indicates **cancer**. Preferred Antibody: The antibody is preferably a monoclonal antibody.

ACTIVITY - Cytostatic; antidiabetic; anti-inflammatory; antiasthmatic; antiarthritic; vulnerary; antibacterial; fungicide; virucide. No supporting data available.

MECHANISM OF ACTION - Gene therapy; hormone; growth factor. No supporting data available.

USE - **Zsig87** polypeptides comprise novel hormones and growth factors that are useful in studying pancreatic cell proliferation or differentiation, insulin, or mammalian cellular metabolism; for promoting wound healing; for treating ovarian, testicular, pancreatic, ocular, immune, lymphatic or blood disorders; in identifying inhibitors or agonists of polypeptide activity; for enhancing fertilization during assisted reproduction in **humans** and animals; as germ-cell specific antigen; in preparing antibodies that bind **zsig87** epitopes, peptides or polypeptides; and for treating diabetes and pancreatic **cancer**. **Zsig87** polypeptides, agonists or antagonists can be used for antimicrobial applications; as cell culture reagents in in vitro studies of exogenous microorganism infection, such as bacterial, viral or fungal infection; to modulate sperm capacitation; to treat disorders associated with, e.g., gonadal development, pregnancy, pubertal changes, menopause, ovarian **cancer**, fertility, ovarian function, polycystic ovarian syndrome, male sexual disorder, testicular or stomach **cancer**; and in inflammatory diseases such as asthma and arthritis (all disclosed). The **Zsig87** polynucleotide can be used in a method to detect **cancer** (claimed). **Zsig87** 87 polynucleotides can be used as probes or primers to clone 5' non-coding regions of a **zsig87** gene, to identify cells, tissues or cell lines which respond to a **zsig87**-stimulated pathway, and in gene therapy.

ADMINISTRATION - Administration is parenteral, particularly intravenous or subcutaneous. Dosage is 0.1-100 microg/kg, preferably 0.5-20 microg/kg per day.

EXAMPLE - Scanning of translated testis, and mast cell library DNA databases using a signal trap as a query resulted in the identification of **expressed** sequence tag sequences that were found to be homologous to a **human** secretory signal sequence. Confirmation of the EST sequence was made by sequence analyses of the cDNA from which the EST originated. This cDNA was contained in a plasmid and was sequenced using standard methods to complete the double stranded sequence of this **clone**. The resulting sequence comprises a fully defined

456 bp sequence given in the specification, and the secreted polypeptide was designated **zsig87** having a sequence of 84 amino acids also given in the specification. (36 pages)

L15 ANSWER 12 OF 21 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN  
ACCESSION NUMBER: 2002-08361 BIOTECHDS

TITLE: Polynucleotides encoding salivary proteins useful as  
**anti-microbial** agents;  
vector-mediated gene transfer and **expression** in  
host cell for **recombinant** protein production and  
gene therapy

AUTHOR: ADLER D A; SHEPPARD P O  
PATENT ASSIGNEE: ZYMOGENETICS INC  
PATENT INFO: US 6331413 18 Dec 2001  
APPLICATION INFO: US 1999-527345 17 Mar 1999  
PRIORITY INFO: US 2000-527345 17 Mar 2000  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 2002-096707 [13]

AB DERWENT ABSTRACT:

NOVELTY - Polynucleotides (I) derived from the 4q12-4q13 region of **human** chromosome 4 and encoding **zsig63** polypeptides, a secreted salivary protein with **anti-microbial** activity, are new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following: (1) an isolated polynucleotide which hybridizes to the 4q12-4q13 region of **human** chromosome 4 under hybridization wash conditions of 0.1 x SSC to 2 x SSC, 0.1% SDS at 55-65 degreesC, and encodes a polypeptide that comprises a sequence of amino acid residues selected from: (a) a defined amino acid sequence (A1) given in the specification from amino acid number 16 (Arg) to amino acid number 37 (Ser); (b) the amino acid sequence A1 from amino acid number 38 (Leu) to amino acid number 126 (Ala); (c) the amino acid sequence A1 from amino acid number 127 (Pro) to amino acid number 219 (Gln); (d) the amino acid sequence A1 from amino acid number 16 (Arg) to amino acid number 219 (Gln); and/or (e) the amino acid sequence A1 from amino acid number 1 (Met) to amino acid number 219 (Gln); (2) an **expression** vector (II) comprising the following operably linked elements: (a) a transcription promoter; (b) a DNA segment wherein said segment hybridizes to the 4q12-4q13 region of **human** chromosome 4 under hybridization wash conditions of 0.1 x SSC to 2 x SSC, 0.1% SDS at 55-65 degreesC encoding a polypeptide comprising the amino acid sequence A1 from amino acid number 16 (Arg) to amino acid number 219 (Gln); and a transcription terminator; (3) a cultured cell (III) into which has been introduced the **expression** vector (II) (the cell **expresses** a polypeptide encoded by the DNA segment); (4) a DNA construct (IV) encoding a fusion protein, the DNA construct comprising: (a) a first DNA segment which hybridizes to the 4q12-4q13 region of **human** chromosome 4 under hybridization wash conditions of 0.1 x SSC to 2 x SSC, 0.1% SDS at 55-65 degreesC encoding a polypeptide selected from the following: (i) the amino acid sequence A1 from residue number 1 (Met) to residue number 15 (Ala); (ii) the amino acid sequence A1 from residue number 16 (Arg) to residue number 219 (Gln); and (b) at least one other DNA segment encoding an additional polypeptide (the first and other DNA segments are connected in-frame, and encode the fusion protein); and (5) a method (V) of producing a **zsig63** polypeptide comprising: (a) culturing the cell (IV); and (b) isolating the **zsig63** polypeptide produced by the cell.

BIOTECHNOLOGY - Preferred Polynucleotides: (I) Comprises a polynucleotide which hybridizes to the 4q12-4q13 region of **human** chromosome 4 under hybridization wash conditions of 0.1 x SSC to 2 x SSC, 0.1% SDS at 55-65 degreesC, selected from: (a) a defined polynucleotide sequence (N1) given in the specification from nucleotide 173 to nucleotide 238; (b) the polynucleotide sequence N1 from nucleotide 239 to

nucleotide 505; (c) the polynucleotide sequence N1 from nucleotide 506 to nucleotide 784; (d) the polynucleotide sequence N1 from nucleotide 173 to nucleotide 784; (e) the polynucleotide sequence N1 from nucleotide 128 to nucleotide 784; and (f) the polynucleotide sequence complementary to (a) through (e). Preferably, (I) comprises nucleotide 1 to nucleotide 657 of a defined nucleotide sequence (N2) given in the specification. Preferred **Expression Vector**: (II) Further comprises a secretory signal sequence operably linked to the DNA segment. Preparation: The nucleic acids were derived from the 4q12-4q13 region of **human** chromosome 4 by standard methodologies.

ACTIVITY - Antimicrobial. No biological data given.

MECHANISM OF ACTION - Gene therapy; Protein therapy.

USE - The polypeptides may be used for the **recombinant** production of **anti-microbial** proteins.

EXAMPLE - Scanning of a translated DNA database resulted in identification of an **expressed** sequence tag (EST) sequence found to be a novel member of the adhesion family and designated **zsig63**. Confirmation of the EST sequence was made by sequence analyses of the cDNA from which the EST originated. This cDNA **clone** was obtained and sequenced using primers: ZC6768, ZC694, ZC7231, ZC7764a. The insert was 1 kb and was full-length. (1 pages)

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TITLE: Secreted and transmembrane polypeptides and **human** nucleic acids encoding them that are overexpressed in cancerous tissues

INVENTOR(S): Baker, Kevin P.; Chen, Jian; Desnoyers, Luc; Goddard, Audrey; Godowski, Paul J.; Gurney, Austin L.; Pan, James; Smith, Victoria; Watanabe, Colin K.; Wood, William I.; Zhang, Zemin

PATENT ASSIGNEE(S): Genentech, Inc., USA

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PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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US 2003166129	A1	20030904	US 2002-176920	20020620
US 2003170798	A1	20030911	US 2002-176490	20020620
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US 2003170801	A1	20030911	US 2002-176983	20020621
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US 2003170806	A1	20030911	US 2002-179521	20020624
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US 2003104543	A1	20030605	US 2002-184657	20020628
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US 2003032138	A1	20030213	US 2002-187885	20020702
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US 2001-274399P	P	20010309
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US 2001-880457	A	20010612
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US 2001-908827	A1	20010718
US 2001-918585	A1	20010730
WO 2001-US25464	W	20010814
WO 2001-US26626	W	20010823
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US 2001-6867	A1	20011206

AB The present invention is directed to novel polypeptides and to nucleic acid mols. encoding those polypeptides. Thus, 305 cDNAs encoding **human** secreted or transmembrane proteins were identified by extracellular domain homol. screening, amylase screening, and signal algorithm anal. These transcripts for these proteins are overexpressed in various cancerous tissues, including adrenal, lung, colon, breast, prostate, rectal, cervical, and liver tumors. Certain of the proteins stimulate release of tumor necrosis factor-.alpha. from **human** blood, and also stimulate proliferation or differentiation of chondrocytes. Also provided herein are vectors and host cells comprising those nucleic acid sequences, chimeric polypeptide mols. comprising the polypeptides of the present invention fused to heterologous polypeptide sequences, antibodies which bind to the polypeptides of the present invention and to methods for producing the polypeptides of the present invention.

L15 ANSWER 14 OF 21 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN  
 ACCESSION NUMBER: 2000-08478 BIOTECHDS

TITLE: **Human** secretory protein 48 polypeptides and polynucleotides useful for promoting leukocyte proliferation and for treating immunosuppressed individuals; production of protein, **Zsig48**, via vector useful for treating **cancer** and HIV virus-1 infection

AUTHOR: Lok S; Sheppard P O  
 PATENT ASSIGNEE: Zymogenetics  
 LOCATION: Seattle, WA, USA.  
 PATENT INFO: WO 2000018796 6 Apr 2000  
 APPLICATION INFO: WO 1999-US22970 1 Oct 1999  
 PRIORITY INFO: US 1998-164740 1 Oct 1998  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 OTHER SOURCE: WPI: 2000-303441 [26]

AB A new protein (I) containing a sequence that is at least 90% identical with the disclosed amino acid sequences is claimed. (I) is a secretory protein, **Zsig48**, which stimulates the proliferation of peripheral blood mononuclear cells. Also claimed are: a protein (II) containing the disclosed amino acid sequences; polynucleotides (Ia) and (IIa), respectively; an antibody (III) which binds to a protein containing a sequence with of 90% identity to the disclosed amino acid sequences; an anti-idiotypic antibody (IV) which binds to an epitope of

(III). Also disclosed are: new variants, antisense sequences and sequences which hybridize to (Ia) and (IIa); **expression** vector containing (Ia) and (IIa); **recombinant** host cells containing the **expression** vector; use of vectors for preparation of (I) and (II); fusion proteins containing a secretion signal sequence and a protein; detecting change in chromosome containing **Zsig48**; diagnosing an alteration in the **Zsig48** gene; and kits for performing diagnostic assays for **Zsig48** gene. (I) is useful for promoting the proliferation of leukocyte and treating **cancer** patients. (I) also useful for treating HIV virus-1 infected individual. (141pp)

L15 ANSWER 15 OF 21 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN  
ACCESSION NUMBER: 2001-03858 BIOTECHDS

TITLE: New **zsig45** polypeptides and polynucleotides for treating or preventing e.g. thyroid, bone or heart disorders, inflammation, **cancer**, viral and bacterial infections;

human recombinant **zsig45**

protein gene useful in gene therapy

AUTHOR: Deisher T A; Sheppard P O

PATENT ASSIGNEE: ZymoGenetics

LOCATION: Seattle, WA, USA.

PATENT INFO: US 6140084 31 Oct 2000

APPLICATION INFO: US 1998-203623 1 Dec 1998

PRIORITY INFO: US 1998-203623 1 Dec 1998

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2001-040302 [05]

AB An isolated polynucleotide encoding a protein at least 90% identical to a disclosed residue amino acid sequence (I, II and III), all fully defined, is new. Also claimed are: an isolated polynucleotide; an **expression** vector containing the disclosed linked element; a culture cell into which has been introduced an **expression** vector; a DNA construct encoding a fusion protein; producing a **zsig45** protein. Also disclosed are: producing an antibody to **zsig45** protein; detecting in a test sample an agonist or antagonist; and fusion proteins or polypeptides containing **zsig45**. The molecules are useful for treating disorders associated with thyroid dysfunction, ischemia, reperfusion injury, inflammatory disorders, osteoporosis, Paget's disease, etc. They are also useful for treating or preventing to treat or prevent development of pathological conditions in thyroid, heart, etc. They may also be used as analgesics for bone pain, to modify inflammation, etc. They can be used for modulating nutrient uptake or energy balance and to prevent various thyroid conditions, etc. The **zsig45** polynucleotides and proteins may be used to identify and isolate receptors involved in thyroid. (37pp)

L15 ANSWER 16 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:493674 HCAPLUS

DOCUMENT NUMBER: 133:130783

TITLE: Cloning of a potential tumor suppressor gene  
**Zsig62** and its therapeutic use

INVENTOR(S): Sheppard, Paul O.; Novak, Julia E.; Raymond, Fenella C.

PATENT ASSIGNEE(S): Zymogenetics, Inc., USA

SOURCE: PCT Int. Appl., 89 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000042183	A2	20000720	WO 2000-US1902	20000118
WO 2000042183	A3	20030508		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-233610 A 19990119

AB Studies indicate that mutations in tumor suppressor genes occur early in the process of carcinogenesis, and that these mutations are correlated with a subsequent development of **cancer**. The detection of such alterations would provide useful mol. markers for diagnosis, surveillance, early tumor identification and intervention, and prognosis. A novel **human** gene, designated as "**Zsig62**", resides within a region of chromosome 16q that is assocd. with prostate and breast **cancer**, and that appears to contain tumor suppressor genes. Like a tumor suppressor gene, the **Zsig62** gene is **expressed** in particular normal tissues, but not in tumors derived from those tissues. Methods of **expressing Zsig62** gene, prepg. its antibody, using **Zsig62** gene and its products for **cancer** diagnosis and therapy are provided.

L15 ANSWER 17 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:753433 HCAPLUS

DOCUMENT NUMBER: 132:441

TITLE: Method for diagnosis and treatment of **cancer** using antagonists, antibodies and antisense nucleotides to secretory protein-9

INVENTOR(S): Moore, Emma E.; Taft, David W.

PATENT ASSIGNEE(S): Zymogenetics, Inc., USA

SOURCE: PCT Int. Appl., 45 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9960405	A1	19991125	WO 1999-US11107	19990519

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RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9940055	A1	19991206	AU 1999-40055	19990519
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PRIORITY APPLN. INFO.: US 1998-81183 19980519

WO 1999-US11107 19990519

AB A method for diagnosing and treating tumors esp. brain, liver, lung, esophageal, stomach, colon, rectal, thyroid, and lymphoma tumors using antagonists, antibodies and antisense nucleotides to secretory protein-9 (**Zsig9**), is claimed. CDNA for **Zsig9** overexpressed in many tumors was **cloned** from **human** and mouse sources. Various forms of the protein corresponding to different post-translational processing and alternative splicing were found in **human** as well



as the mouse ortholog. A nucleic acid probe for testing the **Zsig9** expression was constructed from the **cloned Zsig9** cDNA. Northern blot anal. of various **human** tissues using the constructed probe revealed that the **Zsig9** was strongly **expressed** in heart, placenta, liver, and kidney; intermediate in spleen, thymus, prostate, testis, ovary, small intestine, colon, peripheral blood lymphocytes, thyroid, and spinal cord. A nucleic acid probe was radiolabeled with P32 and was used to detect strong **expression** of **Zsig9** in various **human** tumors: brain, liver, lung, esophageal, stomach, colon, rectal, and thyroid. Based on the strong **expression** of **Zsig9** in many tumors, the use of labeled probe for detecting **human** tumors is proposed. Also, the use of antagonists such as antibodies to **Zsig9** for treating **cancer** is proposed wherein the antagonist is either radiolabeled or fused to a polypeptide toxin. The use of anti-sense polynucleotide probes to inhibit the **expression** of **Zsig9** for treatment of **cancer** is further proposed.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 18 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:595200 HCAPLUS

DOCUMENT NUMBER: 131:210082

TITLE: **Cloning** and cDNA sequences of 90 **human** proteins containing extracellular domains

INVENTOR(S): Wood, William I.; Goddard, Audrey; Gurney, Austin; Yuan, Jean; Baker, Kevin P.; Chen, Jian

PATENT ASSIGNEE(S): Genentech, Inc., USA

SOURCE: PCT Int. Appl., 530 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 113

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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AB The present invention is directed to novel polypeptides and to nucleic acid mols. encoding those polypeptides. The extracellular domain (ECD) sequences (including the secretion signal sequence, if any) from about 950 known secreted proteins were used to search public and proprietary EST databases, and ECD protein sequences with a Blast score of 70 or better were used to assemble consensus sequences and to **clone** and isolate nucleic acids from a cDNA library. The cDNAs contg. full-length open reading frames for 90 ECD-contg. proteins are provided, and in some cases, biol. activities and tissue **expression** profiles detd. Also provided herein are vectors and host cells comprising those nucleic acid sequences, chimeric polypeptide mols. comprising the polypeptides of the present invention fused to heterologous polypeptide sequences, antibodies which bind to the polypeptides of the present invention and to methods for producing the polypeptides of the present invention.

L15 ANSWER 19 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:48800 HCAPLUS

DOCUMENT NUMBER: 130:120475

TITLE: **Cloning** and cDNA sequences of **human** and murine secretory peptide-9 and their overexpression in tumors

INVENTOR(S): Sheppard, Paul O.; Jelinek, Laura J.; Jaspers, Stephen R.; Whitmore, Theodore E.

PATENT ASSIGNEE(S): Zymogenetics, Inc., USA

SOURCE: PCT Int. Appl., 85 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

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AB Novel mammalian secretory polypeptides, polynucleotides encoding the polypeptides (called secretory peptide-9 or **Zsig9**), and related compns. and methods including antibodies and antiidiotypic antibodies. The cDNAs encoding **human** and murine **Zsig9** are provided and sequenced. The potential N-terminal 3-dimensional structure of **Zsig9** should have similarities to that predicted for amylin and calcitonin-gene related peptides. Northern anal. shows that **Zsig9** is ubiquitous with higher levels in placenta, pancreas, thyroid, prostate, and liver. The gene for **Zsig9** maps 344.72 cR 3000 from the top of the **human** chromosome 12 linkage group on the WICGR radiation hybrid map. Overexpression of these proteins is indicative of the presence of **cancer**. Antibodies and antisense nucleotides can be used therapeutically to treat the disease. Furthermore, antibodies to **Zsig9** and nucleotide primers and probes can be used to diagnose the presence of tumors.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 20 OF 21 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN

ACCESSION NUMBER: 1998-11206 BIOTECHDS

TITLE: Secreted novel **zsig**-10 protein;  
with homology to the *Xenopus* cement gland protein used in the treatment, diagnosis and drug screening of a range of diseases e.g. **cancer**, bacterium infection, AIDS, etc.

AUTHOR: Sheppard P O  
PATENT ASSIGNEE: Zymogenetics  
LOCATION: Seattle, WA, USA.  
PATENT INFO: WO 9841627 24 Sep 1998  
APPLICATION INFO: WO 1998-US5251 18 Mar 1998  
PRIORITY INFO: US 1997-39631 19 Mar 1997  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 1998-531566 [45]

AB A novel **human zsig**-10 protein (I) which has homology to *Xenopus* cement gland protein is claimed. Also claimed are: a DNA construct encoding a fusion protein, comprising a secretory signal sequence operably linked to another protein; an **expression** vector comprising a transcription promoter, a DNA sequence (II) encoding (I), and a transcriptional terminator; a host cell containing the **expression** vector, so that it **expresses** (I); an antibody or binding protein specific for an epitope of (I); and a DNA probe or DNA primer composed of at least 14 continuous nucleotides of (II). (I) is believed to have antibiotic, fungicide, etc. activity, mucous-modulating and or adhesion-modulating activity. (I) and (II) can be used in the study and treatment of tumor metastasis, bacterium colonization, susceptibility to and persistence of infection, microbial infection, AIDS, cystic fibrosis, chronic obstructive pulmonary disease, asthma, sinonasal inflammatory disease, inflammatory bowel disease, bronchitis or Crohn disease. The products can also be used for detection, diagnosis and drug screening. (110pp)

L15 ANSWER 21 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:682530 HCAPLUS

DOCUMENT NUMBER: 129:299047

TITLE: **Human** secreted F-spondin homolog and its

INVENTOR(S): cDNA and diagnosis of prostate cancer  
 Sheppard, Paul O.  
 PATENT ASSIGNEE(S): Zymogenetics, Inc., USA  
 SOURCE: PCT Int. Appl., 162 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9845442	A2	19981015	WO 1998-US7117	19980410
WO 9845442	A3	19990114		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9869613	A1	19981030	AU 1998-69613	19980410
PRIORITY APPLN. INFO.:			US 1997-43421P	P 19970410
			US 1997-49288P	P 19970611
			WO 1998-US7117	W 19980410

AB The present invention relates to a secreted protein **expressed** at very high level in prostate tissue and polynucleotides encoding the same. This protein, called **Zsig25**, contains an N-terminal domain with homol. to rat floor plate F-spondin and a C-terminal sequence which appears to be a single thrombospondin type 1 domain. **Zsig25** is believed to be adhesion-modulating and may be used for diagnosis of prostate adenocarcinoma or for sorting cancerous from non-cancerous cells. The present invention also includes antibodies to the **Zsig25**. The **Zsig25** gene was mapped to human chromosome 4p16.3, the region assocd. with Wolf-Hirschhorn syndrome. **Zsig25** with an N-terminal FLAG peptide was produced with BHK 570 cells transformed with **expression** vector zSIG25NF/pZP9. An adenovirus **expression** vector was also prepd. The FLAG-**Zsig25** protein stimulated proliferation of BaF3 and CA-1 cell lines, an interleukin 3-dependent pre-lymphoid cell line derived from bone marrow and another interleukin 3-dependent cell line obtained from lymph nodes of a mouse with B-cell lymphoma.

=> e adler d a/au  
 E1 1 ADLER CYRIL/AU  
 E2 868 ADLER D/AU  
 E3 233 --> ADLER D A/AU  
 E4 25 ADLER D B/AU  
 E5 43 ADLER D C/AU  
 E6 218 ADLER D D/AU  
 E7 14 ADLER D E/AU  
 E8 43 ADLER D G/AU  
 E9 10 ADLER D H/AU  
 E10 3 ADLER D I/AU  
 E11 41 ADLER D J/AU  
 E12 4 ADLER D K/AU

=> s e3  
 L16 233 "ADLER D A"/AU

=> e sheppard p o/au  
 E1 94 SHEPPARD P M/AU

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E2      38      SHEPPARD P N/AU
E3      194 --> SHEPPARD P O/AU
E4      17      SHEPPARD P R/AU
E5      7       SHEPPARD P S/AU
E6      1       SHEPPARD P T/AU
E7      34      SHEPPARD P W/AU
E8      6       SHEPPARD PATRICIA/AU
E9      12      SHEPPARD PATRICIA C/AU
E10     1       SHEPPARD PATRICIA K/AU
E11     1       SHEPPARD PATRICIA KRIM/AU
E12     16      SHEPPARD PAUL/AU

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=> s e3

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L17      194 "SHEPPARD P O"/AU
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=> s l16 or l17

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L18      422 L16 OR L17
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=> d his

(FILE 'HOME' ENTERED AT 11:45:12 ON 30 JAN 2004)

FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS, LIFESCI' ENTERED AT 11:45:38 ON 30 JAN 2004

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L1      6 S "ZSIG63"
L2      4 DUP REM L1 (2 DUPLICATES REMOVED)
L3      146427 S SALIVARY
L4      150 S ZSIG###
L5      12 S L3 AND L4
L6      8 DUP REM L5 (4 DUPLICATES REMOVED)
L7      6346882 S CLON? OR EXPRESS? OR RECOMBINANT
L8      126 S L4 AND L7
L9      100 S HUMAN AND L8
L10     23 S CANCER AND L9
L11     23517 S TRANSCRIPTION(A) ACTIVATION OR ANTI(W) MICROBIAL
L12     4 S L9 AND L11
L13     23517 S L11 OR L12
L14     26 S L12 OR L10
L15     21 DUP REM L14 (5 DUPLICATES REMOVED)
        E ADLER D A/AU
L16     233 S E3
        E SHEPPARD P O/AU
L17     194 S E3
L18     422 S L16 OR L17

```

=> s l4 and l18

```
L19      49 L4 AND L18
```

=> dup rem l19

PROCESSING COMPLETED FOR L19

```
L20      49 DUP REM L19 (0 DUPLICATES REMOVED)
```

=> s l1 and l20

```
L21      4 L1 AND L20
```

=> dup rem l21

PROCESSING COMPLETED FOR L21

```
L22      4 DUP REM L21 (0 DUPLICATES REMOVED)
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=> d 1-4 ibib ab

```

L22  ANSWER 1 OF 4  BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2003-13605  BIOTECHDS
TITLE:      Novel isolated zsig63 polypeptide, member of the

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adhesin family, useful for treating dental carries,  
periodontal disease, thrush, gastrointestinal disease,  
urinary tract infections, vaginal infections, skin infections

vector-mediated gene transfer and expression in host cell  
for recombinant protein production for use in disease  
diagnosis and gene therapy

AUTHOR: ADLER D A; SHEPPARD P O  
PATENT ASSIGNEE: ADLER D A; SHEPPARD P O  
PATENT INFO: US 2002173027 21 Nov 2002  
APPLICATION INFO: US 2001-922469 3 Aug 2001  
PRIORITY INFO: US 2001-922469 3 Aug 2001; US 1999-124820 17 Mar 1999  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 2003-328428 [31]

AB DERWENT ABSTRACT:

NOVELTY - An isolated **zsig63** polypeptide (I) comprising at least 90 % identity to an amino acid sequence which comprises amino acids 16(Arg)-37(Ser) (domain 1 of **zsig63**), 38(Leu)-126(Ala) (domain 2), 127(Pro)-219(Gln) (domain 3), 16(Arg)-219(Gln) (mature **zsig63** polypeptide) or 1(Met)-219(Gln) of a 219 amino acid sequence (S1), given in the specification, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for: (1) an isolated polynucleotide (II) encoding (I); (2) an expression vector (III) comprising the following operably linked elements, a transcription promoter, DNA segment encoding a **zsig63** polypeptide comprising an amino acid sequence that is at least 90 % identical to amino acids 16(Arg)-219(Gln) of (S1), and a transcription terminator; (3) a cultured cell (IV) into which has been introduced (III), where the cell expresses a polypeptide encoded by the DNA segment; (4) a DNA construct (V) encoding a fusion protein, comprising a first DNA segment encoding a polypeptide chosen from amino acid sequence (S1) from residues 1(Met)-15(Ala), 16(Arg)-37(Ser), 38(Leu)-126(Ala), 127(Pro)-219(Gln), 16(Arg)-219(Gln), and at least one other DNA segment encoding an additional polypeptide, where the first and other DNA segments are connected in-frame, and encode the fusion protein; (5) a fusion protein (VI) produced by culturing a host cell into which has been introduced a vector comprising operably linked transcriptional promoter, (V), and transcriptional terminator, and recovering the protein encoded by the DNA segment; (6) producing (I); (7) detecting in a test sample, the presence of agonist of **zsig63** protein activity, comprising: (a) transfecting a **zsig63**-responsive cell with a reporter gene construct that is responsive to **zsig63**-stimulated cellular pathway, adding a test sample; and (b) comparing levels of response in the presence and absence of the test sample, by a biological or biochemical assay, and determining from the comparison, the presence of the agonist of **zsig63** activity in the sample; (8) producing an antibody to **zsig63** polypeptide, which involves inoculating an animal with a polypeptide consisting of 9-204 amino acids, which consists of a contiguous sequence of amino acids in (S1) from amino acids 16(Ala)-219(Gln), (I), and a polypeptide comprising amino acids 16(Arg)-37(Ser), 38(Leu)-126(Ala), 127(Pro)-219(Gln), 16(Arg)-219(Gln), 1(Met)-219(Gln), 14(Phe)-19(Arg), 16(Arg)-21(Phe), 24(Gly)-29(Asp), 25(Glu)-30(Asp), 187(Glu)-192(Glu), 24(Gly)-33(Pro), 17(Lys)-33(Pro), 66(Thr)-73(Pro), 103(Pro)-108(Gly), 190(Ala)-197(Glu), 202(Lys)-215(Gly) or 190(Ala)-215(Glu) of (S1), where the polypeptide elicits an immune response in the animal to produce the antibody, and isolating the antibody from the animal; (9) an antibody (VII) produced by the method of (8), which binds to (I); and (10) an antibody (VIII) that binds to (I).

WIDER DISCLOSURE - (1) counterpart polypeptides and polynucleotides of **zsig63**; (2) allelic and splice variants of (S1) and (S2); (3) functional fragments of (I) and the polynucleotides encoding the fragments; (4) identifying agonist and antagonist of **zsig63** polypeptide using a microphysiometer; and (5) mice engineered to express

**zsig63** gene referred to as transgenic mice, and mice that exhibit complete absence of **zsig63** gene function referred to as knockout mice.

**BIOTECHNOLOGY** - Preparation: (I) is produced by culturing (IV) and isolating the polypeptide produced by the cell (claimed). Preferred Polynucleotide: (I), preferably comprises an amino acid sequence which comprises amino acid residues 16(Arg)-37(Ser), 38(Leu)-126(Ala), 127(Pro)-219(Gln), 16(Arg)-219(Gln) or 1(Met)-219(Gln) of (S1). (II) nucleotides 173-784 or 128-784 of a 1008 nucleotide sequence (S2), given in the specification, or a polynucleotide sequence complementary to the sequence. Optionally, (II) comprises nucleotides 1-657 of a fully defined degenerate sequence of (S1) which has 657 nucleotides, given in the specification. Preferred Vector: (III) further comprises a secretory signal sequence operably linked to the DNA segment. Preferred Antibody: (VII) is a monoclonal antibody.

**ACTIVITY** - Antimicrobial; Antibacterial; Vulnerary. No biological data is given.

**MECHANISM OF ACTION** - Gene therapy.

**USE** - (I) is useful for detecting in a test sample, the presence of antagonist of **zsig63** protein activity, which involves transfecting a **zsig63**-responsive cell with a reporter gene construct that is responsive to **zsig63**-stimulated cellular pathway, and producing (I) by recombinant techniques, and adding (I) to the cell in the presence and absence of the test sample, and comparing level of response to the polypeptide in the presence and absence of the test sample, by a biological or biochemical assay, and determining from the comparison, the presence of the antagonist of **zsig63** activity in the sample. (IV) is useful for producing (I) by standard recombinant methods. (All claimed.) (I) comprises 16 full evenly-spaced coil-like repeats in domain 2. The coil-like repeats are useful for identifying new family members. (I) and (II) are useful for identifying and isolating receptors that bind to **zsig63** polypeptide. (I) has antimicrobial activity and since exhibits high expression in salivary gland, can be used for treating dental carries, periodontal disease, thrush, and gastrointestinal disease, urinary tract infections, vaginal infections, skin infections and other epithelial wounds. The polypeptides can be used to establish normal microflora and protect against pathogenic colonization and invasion. (I) can also be used for providing pro-inflammatory activity for treating chronic, tissue damage particularly in areas having limited or damaged vascular system, e.g. damage in extremities associated with diabetes. (I) is also useful for treating conditions where stimulation of immune responsiveness is desired, e.g. AIDS patient or in individuals that have undergone chemotherapy, radiation treatment, etc. (I) is also useful for treating lung infections associated with cystic fibrosis. (I) is useful for studying chemoattraction of monocytes in cell culture, studying activity of melanocortin family of receptors in cell culture, studying ion flux in cell culture, studying cytotoxic activity in mammalian cell such as tumor cells in cell culture, as cell culture reagents in in vitro studies of exogenous microorganism infection such as bacterial, viral or fungal infections, and for studying epithelial cell defensin induction in cell culture. (I) is useful as a diagnostic reagent e.g. **zsig63** polypeptide is detected in the serum or tissue biopsy of a patient, for evaluating salivary gland function or dysfunction (e.g. digestive dysfunction, wound healing dysfunction, inadequate saliva production or composition, mucosal integrity breakdown, and failure or diminished anti-microbial function. Detection of **zsig63** polypeptide at relatively high levels in the trachea may indicate that such polypeptides may serve as a marker of lung dysfunction. (I) is also useful as a diagnostic reagent for conditions associated with salivary gland or lung dysfunction including salivary gland carcinoma, Pneumocystis carinii infection (particularly associated with AIDS patient), emphysema, chronic bronchitis, etc. (I) is also useful for diagnosing prostate dysfunctions such as prostate adenocarcinoma. (I) is useful for aiding digestion, and



as components of defined cell culture media and may be used alone or in combination with other cytokines and hormones to replace serum that is commonly used in culture. The **zsig63** polypeptides are useful as research reagent such as for the expansion of cultured cells, and as immunogen to prepare anti-**zsig63** antibodies. (II) is useful in gene therapy applications to increase or inhibit **zsig63** activity, and for detecting abnormalities on human chromosome 4 associated with disease or other human traits. **Zsig63** polynucleotide probes can be used to detect abnormalities or genotypes associated with genes located at the 4q12-4q13 region of chromosome 4, e.g. dentinogenesis imperfecta, and dentin dysplasia type II.

ADMINISTRATION - (I) is administered by topical, inhalant, parenteral, preferably intravenous or subcutaneous delivery. No dosages is given.

EXAMPLE - Scanning of a translated DNA database resulted in identification of an expressed sequence tag (EST) sequence found to be a novel member of the adhesin family and designated **zsig63**. Confirmation of the EST sequence was made by sequence analyses of the cDNA from which the EST originated. This cDNA clone was obtained and sequenced. Northern blot tissue distribution of the mRNA revealed high expression in salivary gland, and moderate to high expression in thyroid. (32 pages)

L22 ANSWER 2 OF 4 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN

ACCESSION NUMBER: 2003-01837 BIOTECHDS

TITLE: Novel secreted salivary polypeptide, **zsig63**, useful as antimicrobial agent for treating microbial infection, dental carries, periodontal disease, thrush gastrointestinal disease, and for aiding digestion; recombinant protein production and agonist and antagonist use in disease therapy and gene therapy

AUTHOR: ADLER D A; SHEPPARD P O

PATENT ASSIGNEE: ADLER D A; SHEPPARD P O

PATENT INFO: US 2002090677 11 Jul 2002

APPLICATION INFO: US 2001-923236 3 Aug 2001

PRIORITY INFO: US 2001-923236 3 Aug 2001; US 1999-124820 17 Mar 1999

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2002-642378 [69]

AB DERWENT ABSTRACT:

NOVELTY - An isolated secreted salivary polypeptide (I) designated as **zsig63**, comprising an amino acid sequence 90% identical to a sequence (S1) of 1 (Met)-219 (Gln) fully defined in the specification, 16 (Arg)-37 (Ser), 38 (Leu)-126 (Ala), 127 (Pro)-219 (Gln) or 16 (Arg)-219 (Gln) of (S1), is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) an isolated polynucleotide (II) encoding (I); (2) an expression vector (III) comprising a transcription promoter, a DNA segment encoding a **zsig63** polypeptide comprising an amino acid sequence that is 90% identical to (S1) from amino acid 16 (Arg)-219 (Gln) and a transcription terminator, operably linked to each other; (3) a cultured cell (IV) containing (III), expresses a polypeptide encoded by the DNA segment; (4) a DNA construct (V) encoding a fusion protein, comprises a first DNA segment encoding a polypeptide comprising an amino acid sequence of 1 (Met)-15 (Ala), 16 (Arg)-37 (Ser), 38 (Leu)-126 (Ala), 127 (Pro)-219 (Gln) or 16 (Arg)-219 (Gln) of (S1), and at least one other DNA segment encoding an additional polypeptide, where the first and other DNA segments are connected in-frame and encode the fusion protein; (5) a fusion protein produced by culturing a host cell comprising a vector having transcriptional promoter, (V), a transcriptional terminator, operably linked to each other and recovering the protein encoded by the DNA segment, is introduced; (6) producing (I); (7) detecting in a test sample, the presence of an agonist or antagonist of **zsig63** protein activity, involves transfecting a **zsig63**-responsive

cell, with a reporter gene construct that is responsive to a **zsig63**-stimulated cellular pathway and producing a **zsig63** polypeptide by the culturing the cell, and adding the **zsig63** polypeptide to the cell in the presence and absence of a test sample and comparing levels of response to the **zsig63** polypeptide, in the presence and absence of the test sample, by a biological or biochemical assay and determining from the comparison, the presence of the agonist or antagonist of **zsig63** activity in the test sample; (8) producing an antibody to **zsig63** polypeptide, involves inoculating animal with polypeptides consisting of 9 to 204 amino acids, the polypeptide consist of a contiguous sequence of amino acids in (S1) from amino acid 16 (Ala) to amino acid number 219 (Gln), (I), or a polynucleotide comprising 14 (Phe)-19 (Arg), 16 (Arg)-21 (Phe), 24 (Gly)-29(Asp), 25 (Glu)-30(Asp), 187 (Glu)-192 (Glu), 24 (Gly)-33 (Pro), 17 (Lys)-33 (Pro), 66 (Thr)-73 (Pro), 102 (Pro)-108 (Gly), 180 (Ala)-197 (Glu), 202 (Lys)-215 (Gly), 190 (Ala)-215 (Glu) of (S1), where the polypeptide elicits an immune response in the animal to produce the antibody, and isolating the antibody from the animal; and (9) an antibody (Ab) produced by the above method which binds to a **zsig63** polypeptide or (I).

WIDER DISCLOSURE - Also disclosed are: (1) a **zsig63** polypeptide-encoding polynucleotides comprising a sequence of 657 nucleotides fully defined in the specification; (2) fragments of a sequence of 1008 nucleotides fully defined in the specification; (3) orthologs, variant or functional fragment of (I) and (II); (4) nucleic acid molecule encoding functional fragment of (I); (5) a pharmaceutical composition comprising (I); and (6) reagent comprising **zsig63** gene, a probe comprising **zsig63** DNA or RNA or a subsequence for diagnostic application.

BIOTECHNOLOGY - Preparation: (I) is produced by culturing (IV) and isolating (I) produced by the cell. Preferred Vector: (III) further comprises a secretory signal sequence operably linked to the DNA segment. Preferred Antibody: Ab is a monoclonal antibody.

ACTIVITY - Antibacterial; Fungicide; Virucide; Antiinflammatory; Antiarteriosclerotic; Vasotropic; Anorectic. No biological data provided.

MECHANISM OF ACTION - Gene therapy; Modulator of (I). No supporting data provided.

USE - (I) is useful as a host defense polypeptide, immune modulating factor, antipathogenic polypeptide, cell-cell signaling molecule, growth factor, cytokine, or as secreted extracellular matrix associated proteins with growth factor hormone activity. (I) is useful for treating conditions associated with pathological microbes, including bacterial, fungal, and viral infections, for treating dental carries (tooth decay), periodontal disease, thrush, and gastrointestinal disease, for treating urinary tract infection, vaginal infection, and for preventing infection in skin and other epithelial wounds. (I) is useful for establishing normal microflora and protect against pathogenic colonization and invasion, for treating chronic tissue damage e.g. damage in extremities associated with diabetes, and useful as anti-inflammatory agents. (I) is useful as a marker of lung dysfunction, salivary gland dysfunction, or dysfunction of prostate gland. (I) is therapeutically useful for aiding digestion. (I) is useful as a research reagent for the expansion of cultured cells, to prepare antibodies that bind to **zsig63** epitopes, peptides or polypeptides, as antigen to inoculate an animal for eliciting an immune response. **zsig63** is useful for identifying cells, tissues or cell lines which respond to **zsig63**-stimulated pathway, or for identifying inhibitors of its activity. (I) is useful for studies to isolate mesenchymal stem cells and myocyte or other progenitor cells both in vivo and ex vivo, and serve as an additional cell surface or secreted marker associated with stage-specific expression of a tissue. (II) is useful in gene therapy for increasing or inhibiting **zsig63** activity, for detecting abnormalities on human chromosome 4 associated with disease or other human traits and as diagnostics in forensic DNA profiling. (I) or Ab is useful for studying chemoattraction of monocytes, for studying the activity of the melanocortin family of

receptors, for studying or evaluating ligand or putative ligand binding and/or ion flux (calcium flux, potassium flux, sodium flux) regulation or modulation, for studying cytotoxic activity against mammalian cells, as cell culture reagent in in vitro studies of exogenous microorganism infection, and in in vivo animal models of infection. (I) or Ab is useful for identifying and isolating receptors for **zsig63**. Ab is useful for detecting **zsig63** polypeptides in the serum or tissue biopsy of a patient undergoing evaluation for salivary gland function or dysfunction. Ab is useful for tagging cells that express **zsig63**, for isolating **zsig63** for diagnostic assays for determining circulating levels of **zsig63** polypeptides, for detecting or quantitating soluble **zsig63** as marker of underlying pathology or disease, in analytical methods employing fluorescence activated cell sorting (FACS), for screening expression libraries, for generating anti-idiotypic antibodies, as neutralizing antibodies or as antagonists to block **zsig63** activity in vitro or in vivo, and in in vitro detection of denatured **zsig63** or its fragments in assays. (I), (II) or Ab is useful for stimulating proliferation or differentiation of cardiac myocytes, for proliferation or differentiation of adipocytes and for inhibiting chondrosarcomas, atherosclerosis, restenosis and obesity.

ADMINISTRATION - Pharmaceutical composition comprising (I) is administered through topical, inhalation, parenteral, intravenous or subcutaneous route. Dosage not specified.

EXAMPLE - Full-length **zsig63** was obtained using an expressed sequence tag (EST) sequence. Scanning of a translated DNA database resulted in identification of EST sequence found to be a novel member of the adhesion family and designated **zsig63**. Confirmation of EST sequence was made by sequence analyses of the cDNA from the EST originated. This cDNA clone was obtained and sequenced using the ZC6768 (gcaattaaccctcactaaaggggaac), ZC694 (taatacgactcactataggg), ZC7231 (tttttttttttttttttttttttttttttv), ZC7764a (tttttttttttttttttttttttttta). The insert was about 1 kb and was full-length. (33 pages)

L22 ANSWER 3 OF 4 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN

ACCESSION NUMBER: 2003-01808 BIOTECHDS

TITLE: Novel secreted salivary protein, **zsig63** and polynucleotide encoding it useful for treating microbial infections, inflammatory conditions, dental caries and lung infections associated with cystic fibrosis; vector-mediated gene transfer and expression in host cell for recombinant protein production, drug screening and gene therapy

AUTHOR: ADLER D A; SHEPPARD P O

PATENT ASSIGNEE: ADLER D A; SHEPPARD P O

PATENT INFO: US 2002081701 27 Jun 2002

APPLICATION INFO: US 2001-922480 3 Aug 2001

PRIORITY INFO: US 2001-922480 3 Aug 2001; US 1999-124820 17 Mar 1999

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2002-635468 [68]

AB DERWENT ABSTRACT:

NOVELTY - An isolated **zsig63** (I), a secreted salivary protein comprising a sequence of amino acid residues that is at least 90% identical to a sequence (S1) of 219 amino acids given in the specification, or amino acids 16-37, 38-126, 127-219 or 16-219 of (S1), is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) an isolated polynucleotide (II) encoding (I); (2) an expression vector (III) comprising a DNA segment encoding **zsig63** polypeptide comprising an amino acid sequence that is 90% identical to amino acids 16-219 of (S1), and transcription promoter and terminator; (3) a cultured cell (IV) into which has been introduced (III), where the cell expresses a polypeptide encoded by the DNA segment; (4) a DNA

construct encoding a fusion protein, comprising a first DNA segment encoding amino acids 1-15, 16-37, 38-126, 127-219 or 16-219 of (S1), and at least one other DNA segment encoding an additional polypeptide, where the first and other DNA segments are connected in-frame and encode the fusion protein; (5) a fusion protein produced by culturing a host cell into which has been introduced a vector comprising the above DNA construct and transcription promoter and terminator; (6) producing **zsig63** polypeptide; and (7) an antibody (V) produced using (I), that binds to (I).

**BIOTECHNOLOGY - Preparation:** (I) is produced by culturing (IV) and isolating the polypeptide produced by the cell (claimed). **Preferred Polypeptide:** (I) comprises amino acids 16-37, 38-126, 127-219, 16-219 or 1-219 of (S1). **Preferred Polynucleotide:** (II) comprises a polynucleotide sequence (or its complement) comprising nucleotides 173-784 or 128-784 of a sequence (S2) of 1008 bp given in the specification. **Preferred Vector:** (III) further comprises a secretory signal sequence operably linked to the DNA segment. **Preferred Antibody:** (V) is a monoclonal antibody.

**ACTIVITY - Antibacterial; Fungicide; Virucide; Vulnerary; Anti-HIV; Antiinflammatory.** No supporting data given.

**MECHANISM OF ACTION - Gene therapy.** No supporting data given.

**USE -** (I) is useful for detecting in a test sample, the presence of an antagonist or agonist of **zsig63** protein activity. The method comprises transfecting a **zsig63**-responsive cell with a reporter gene construct that is responsive to a **zsig63**-stimulated cellular pathway, adding the **zsig63** polypeptide to the cell, in the presence and absence of the test sample, comparing the levels of response to the **zsig63** polypeptide in the presence and absence of the test sample, by a biological or biochemical assay, and determining from the comparison, the presence of the antagonist or agonist of **zsig63** activity in the test sample. (I) is also useful as an immunogen for producing an antibody to **zsig63** polypeptide, by inoculating an animal with (I), or its fragment comprising amino acids 9-204, 14-19, 16-21, 24-29, 25-30, 187-192, 24-33, 17-33, 66-73, 103-108, 190-197, 202-215, or 190-215 of (S1) and isolating the antibody from the animal (all claimed). **zsig63**-cytokine fusion proteins or antibody-cytokine fusion protein are useful for enhancing in vivo killing of target tissues. Pharmaceutical composition comprising purified **zsig63** polypeptide are useful in the treatment of conditions associated with pathological microbes, including bacterial, fungal and viral infections. High expression of **zsig63** in salivary gland suggests that anti-microbial polypeptides are useful for treatment of dental caries (tooth decay), periodontal disease, thrush and gastrointestinal disease. Other applications can be used in urinary tract infections, vaginal infections, prevention of infection in skin and other epithelial wounds. The polypeptides can be used to establish normal microflora and protect against pathogenic colonization and invasion. (I) is useful when pro-inflammatory activity is desired. Applications for such pro-inflammatory activity include the treatment of chronic tissue damage, particularly in areas having a limited or damaged vascular system e.g., damage in extremities associated with diabetes. Antagonists to **zsig63** polypeptides may be useful as anti-inflammatory agents. (I) is useful for the treatment of patients having incompetent immune system, such as AIDS patients or individuals that have undergone chemotherapy, radiation treatment. (I) is also useful for the treatment of lung infections associated with cystic fibrosis, for studying chemoattraction of monocytes in cell culture, for studying activity of the melanocortin family of receptors and ion flux in cell culture, and cytotoxic activity against mammalian cells. (I), its fragments, fusion proteins, or agonists are useful as cell culture reagents in in vitro studies of exogenous microorganism infection, such as bacterial, viral or fungal infection and also in in vivo animal models of infection. (I), its agonists or antagonists are useful for aiding digestion. **zsig63** is also useful to identify cells, tissues or cell lines which respond to a **zsig63**-stimulated pathway, to identify and isolate receptors

for **zsig63** and in diagnostic applications. The diagnostic methods are useful in genetic linkage analysis, to detect a genetic abnormality or aberration in a patient. (V) is useful for detecting **zsig63** polypeptides.

ADMINISTRATION - Administered by topical, inhalant or parenteral, particularly intravenous or subcutaneous route. Dosage not specified.

EXAMPLE - Scanning of a translated DNA database resulted in identification of an expressed sequence tag (EST) sequence found to be a novel member of the adhesion family and designated **zsig63**.

Confirmation of the EST sequence was made by sequence analyses of 25 the cDNA from which the EST originated. This cDNA clone was obtained and sequenced using the following primers ZC6768 (gcaattaaccctcactaaaggggaac, ZC694 (taatacgcactcactataggg), ZC7231 (tttttttttttttttttttttttttttv) and ZC7764a (tttttttttttttttttttttttttta). The insert was about 1 kb and was full-length. **Zsig63** was mapped to chromosome 4. (33 pages)

L22 ANSWER 4 OF 4 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN

ACCESSION NUMBER: 2002-08361 BIOTECHDS

TITLE: Polynucleotides encoding salivary proteins useful as anti-microbial agents;  
vector-mediated gene transfer and expression in host cell for recombinant protein production and gene therapy

AUTHOR: ADLER D A; SHEPPARD P O

PATENT ASSIGNEE: ZYMOGENETICS INC

PATENT INFO: US 6331413 18 Dec 2001

APPLICATION INFO: US 1999-527345 17 Mar 1999

PRIORITY INFO: US 2000-527345 17 Mar 2000

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2002-096707 [13]

AB DERWENT ABSTRACT:

NOVELTY - Polynucleotides (I) derived from the 4q12-4q13 region of human chromosome 4 and encoding **zsig63** polypeptides, a secreted salivary protein with anti-microbial activity, are new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following: (1) an isolated polynucleotide which hybridizes to the 4q12-4q13 region of human chromosome 4 under hybridization wash conditions of 0.1 x SSC to 2 x SSC, 0.1% SDS at 55-65 degreesC, and encodes a polypeptide that comprises a sequence of amino acid residues selected from: (a) a defined amino acid sequence (A1) given in the specification from amino acid number 16 (Arg) to amino acid number 37 (Ser); (b) the amino acid sequence A1 from amino acid number 38 (Leu) to amino acid number 126 (Ala); (c) the amino acid sequence A1 from amino acid number 127 (Pro) to amino acid number 219 (Gln); (d) the amino acid sequence A1 from amino acid number 16 (Arg) to amino acid number 219 (Gln); and/or (e) the amino acid sequence A1 from amino acid number 1 (Met) to amino acid number 219 (Gln); (2) an expression vector (II) comprising the following operably linked elements: (a) a transcription promoter; (b) a DNA segment wherein said segment hybridizes to the 4q12-4q13 region of human chromosome 4 under hybridization wash conditions of 0.1 x SSC to 2 x SSC, 0.1% SDS at 55-65 degreesC encoding a polypeptide comprising the amino acid sequence A1 from amino acid number 16 (Arg) to amino acid number 219 (Gln); and a transcription terminator; (3) a cultured cell (III) into which has been introduced the expression vector (II) (the cell expresses a polypeptide encoded by the DNA segment); (4) a DNA construct (IV) encoding a fusion protein, the DNA construct comprising: (a) a first DNA segment which hybridizes to the 4q12-4q13 region of human chromosome 4 under hybridization wash conditions of 0.1 x SSC to 2 x SSC, 0.1% SDS at 55-65 degreesC encoding a polypeptide selected from the following: (i) the amino acid sequence A1 from residue number 1 (Met) to residue number 15 (Ala); (ii) the amino acid sequence A1 from residue number 16 (Arg) to residue number 219 (Gln); and (b) at least one other DNA segment encoding an additional polypeptide (the first and other DNA segments are connected in-frame, and

encode the fusion protein); and (5) a method (V) of producing a **zsig63** polypeptide comprising: (a) culturing the cell (IV); and (b) isolating the **zsig63** polypeptide produced by the cell.

BIOTECHNOLOGY - Preferred Polynucleotides: (I) Comprises a polynucleotide which hybridizes to the 4q12-4q13 region of human chromosome 4 under hybridization wash conditions of 0.1 x SSC to 2 x SSC, 0.1% SDS at 55-65 degreesC, selected from: (a) a defined polynucleotide sequence (N1) given in the specification from nucleotide 173 to nucleotide 238; (b) the polynucleotide sequence N1 from nucleotide 239 to nucleotide 505; (c) the polynucleotide sequence N1 from nucleotide 506 to nucleotide 784; (d) the polynucleotide sequence N1 from nucleotide 173 to nucleotide 784; (e) the polynucleotide sequence N1 from nucleotide 128 to nucleotide 784; and (f) the polynucleotide sequence complementary to (a) through (e). Preferably, (I) comprises nucleotide 1 to nucleotide 657 of a defined nucleotide sequence (N2) given in the specification. Preferred Expression Vector: (II) Further comprises a secretory signal sequence operably linked to the DNA segment. Preparation: The nucleic acids were derived from the 4q12-4q13 region of human chromosome 4 by standard methodologies.

ACTIVITY - Antimicrobial. No biological data given.

MECHANISM OF ACTION - Gene therapy; Protein therapy.

USE - The polypeptides may be used for the recombinant production of anti-microbial proteins.

EXAMPLE - Scanning of a translated DNA database resulted in identification of an expressed sequence tag (EST) sequence found to be a novel member of the adhesion family and designated **zsig63**. Confirmation of the EST sequence was made by sequence analyses of the cDNA from which the EST originated. This cDNA clone was obtained and sequenced using primers: ZC6768, ZC694, ZC7231, ZC7764a. The insert was 1 kb and was full-length. (1 pages)

=> d his

(FILE 'HOME' ENTERED AT 11:45:12 ON 30 JAN 2004)

FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS, LIFESCI' ENTERED AT 11:45:38 ON 30 JAN 2004

```
L1          6 S "ZSIG63"
L2          4 DUP REM L1 (2 DUPLICATES REMOVED)
L3         146427 S SALIVARY
L4          150 S ZSIG###
L5          12 S L3 AND L4
L6           8 DUP REM L5 (4 DUPLICATES REMOVED)
L7         6346882 S CLON? OR EXPRESS? OR RECOMBINANT
L8          126 S L4 AND L7
L9          100 S HUMAN AND L8
L10         23 S CANCER AND L9
L11        23517 S TRANSCRIPTION(A) ACTIVATION OR ANTI(W)MICROBIAL
L12         4 S L9 AND L11
L13        23517 S L11 OR L12
L14         26 S L12 OR L10
L15         21 DUP REM L14 (5 DUPLICATES REMOVED)
              E ADLER D A/AU
L16        233 S E3
              E SHEPPARD P O/AU
L17        194 S E3
L18        422 S L16 OR L17
L19        49 S L4 AND L18
L20        49 DUP REM L19 (0 DUPLICATES REMOVED)
L21         4 S L1 AND L20
L22         4 DUP REM L21 (0 DUPLICATES REMOVED)
```

=> d 1-49 ibib

L22 ANSWER 1 OF 4 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN  
 ACCESSION NUMBER: 2003-13605 BIOTECHDS  
 TITLE: Novel isolated **zsig63** polypeptide, member of the  
 adhesin family, useful for treating dental carries,  
 periodontal disease, thrush, gastrointestinal disease,  
 urinary tract infections, vaginal infections, skin infections  
 ;  
 vector-mediated gene transfer and expression in host cell  
 for recombinant protein production for use in disease  
 diagnosis and gene therapy  
 AUTHOR: **ADLER D A; SHEPPARD P O**  
 PATENT ASSIGNEE: ADLER D A; SHEPPARD P O  
 PATENT INFO: US 2002173027 21 Nov 2002  
 APPLICATION INFO: US 2001-922469 3 Aug 2001  
 PRIORITY INFO: US 2001-922469 3 Aug 2001; US 1999-124820 17 Mar 1999  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 OTHER SOURCE: WPI: 2003-328428 [31]

L22 ANSWER 2 OF 4 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN  
 ACCESSION NUMBER: 2003-01837 BIOTECHDS  
 TITLE: Novel secreted salivary polypeptide, **zsig63**, useful  
 as antimicrobial agent for treating microbial infection,  
 dental carries, periodontal disease, thrush gastrointestinal  
 disease, and for aiding digestion;  
 recombinant protein production and agonist and antagonist  
 use in disease therapy and gene therapy  
 AUTHOR: **ADLER D A; SHEPPARD P O**  
 PATENT ASSIGNEE: ADLER D A; SHEPPARD P O  
 PATENT INFO: US 2002090677 11 Jul 2002  
 APPLICATION INFO: US 2001-923236 3 Aug 2001  
 PRIORITY INFO: US 2001-923236 3 Aug 2001; US 1999-124820 17 Mar 1999  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 OTHER SOURCE: WPI: 2002-642378 [69]

L22 ANSWER 3 OF 4 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN  
 ACCESSION NUMBER: 2003-01808 BIOTECHDS  
 TITLE: Novel secreted salivary protein, **zsig63** and  
 polynucleotide encoding it useful for treating microbial  
 infections, inflammatory conditions, dental caries and lung  
 infections associated with cystic fibrosis;  
 vector-mediated gene transfer and expression in host cell  
 for recombinant protein production, drug screening and  
 gene therapy  
 AUTHOR: **ADLER D A; SHEPPARD P O**  
 PATENT ASSIGNEE: ADLER D A; SHEPPARD P O  
 PATENT INFO: US 2002081701 27 Jun 2002  
 APPLICATION INFO: US 2001-922480 3 Aug 2001  
 PRIORITY INFO: US 2001-922480 3 Aug 2001; US 1999-124820 17 Mar 1999  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 OTHER SOURCE: WPI: 2002-635468 [68]

L22 ANSWER 4 OF 4 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN  
 ACCESSION NUMBER: 2002-08361 BIOTECHDS  
 TITLE: Polynucleotides encoding salivary proteins useful as  
 anti-microbial agents;  
 vector-mediated gene transfer and expression in host cell  
 for recombinant protein production and gene therapy  
 AUTHOR: **ADLER D A; SHEPPARD P O**  
 PATENT ASSIGNEE: ZYMOGENETICS INC  
 PATENT INFO: US 6331413 18 Dec 2001

APPLICATION INFO: US 1999-527345 17 Mar 1999  
PRIORITY INFO: US 2000-527345 17 Mar 2000  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 2002-096707 [13]

=> d 120 1-49 ibib

L20 ANSWER 1 OF 49 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN  
ACCESSION NUMBER: 2003-25983 BIOTECHDS  
TITLE: New **Zsig67** polypeptide which is a member of the  
human secretin-glucagon-VIP hormone family, useful in  
immunological diagnostic assay for **Zsig67** gene  
expression;  
vector-mediated gene transfer and expression in host cell  
for recombinant protein production and gene therapy  
AUTHOR: **SHEPPARD P O**; SHOEMAKER K E; TACKETT M L; JASPERS S  
R  
PATENT ASSIGNEE: SHEPPARD P O; SHOEMAKER K E; TACKETT M L; JASPERS S R  
PATENT INFO: US 2003166156 4 Sep 2003  
APPLICATION INFO: US 2002-82838 21 Feb 2002  
PRIORITY INFO: US 2002-82838 21 Feb 2002; US 1999-116416 19 Jan 1999  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 2003-720929 [68]

L20 ANSWER 2 OF 49 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN  
ACCESSION NUMBER: 2003-27337 BIOTECHDS  
TITLE: New isolated polypeptide of the cystine knot family,  
designated **zsig51**, potentially useful for treating  
and diagnosing diseases associated with the pancreas or  
pituitary gland including diabetes and cancer;  
involving vector-mediated gene transfer and expression in  
host cell for use in diabetes, cancer and gynecological  
disorder diagnosis and therapy  
AUTHOR: **SHEPPARD P O**; LOK S  
PATENT ASSIGNEE: ZYMOGENETICS INC  
PATENT INFO: US 6573363 3 Jun 2003  
APPLICATION INFO: US 1999-250124 12 Feb 1999  
PRIORITY INFO: US 1999-250124 12 Feb 1999; US 1998-74682 13 Feb 1998  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 2003-764576 [72]

L20 ANSWER 3 OF 49 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN  
ACCESSION NUMBER: 2002-09249 BIOTECHDS  
TITLE: New polypeptides which include cytokines, growth factors and  
secreted proteins, useful for modulating immune reaction and  
inflammation and preventing or treating pancreatic disorders,  
diabetes and degenerative diseases;  
recombinant fusion protein production and purification by  
affinity chromatography, useful for antisense gene  
therapy, diagnosis, transgenic animal, feedstuff, antibody  
production, mapping and drugdesign  
AUTHOR: **SHEPPARD P O**; PRESNELL S R; TAFT D W  
PATENT ASSIGNEE: ZYMOGENETICS INC  
PATENT INFO: WO 2002002626 10 Jan 2002  
APPLICATION INFO: WO 2000-US20847 30 Jun 2000  
PRIORITY INFO: US 2000-215446 30 Jun 2000  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 2002-154728 [20]



L20 ANSWER 4 OF 49 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN  
ACCESSION NUMBER: 2003-14671 BIOTECHDS  
TITLE: New **Zsig86** polypeptides and nucleic acid molecules  
useful for treating disorder associated with gonadal  
development, fertility, male sexual dysfunction, impotency,  
prostate/testicular/colon cancer, gastrointestinal mobility;  
recombinant protein production, its encoding gene and  
antibody useful for gene therapy  
AUTHOR: **SHEPPARD P O**; VU T Q; FELDHAUS A L; HALDEMAN B A  
PATENT ASSIGNEE: SHEPPARD P O; VU T Q; FELDHAUS A L; HALDEMAN B A  
PATENT INFO: US 2002192777 19 Dec 2002  
APPLICATION INFO: US 2001-639 1 Nov 2001  
PRIORITY INFO: US 2001-639 1 Nov 2001; US 2000-245070 1 Nov 2000  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 2003-352712 [33]

L20 ANSWER 5 OF 49 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN  
ACCESSION NUMBER: 2003-13622 BIOTECHDS  
TITLE: New pancreatic and ovarian **zsig58** polypeptides  
useful for diagnosing or treating disorders associated with  
gonadal development, pregnancy, pubertal changes, menopause,  
ovarian cancer, fertility, and ovarian or pancreatic function  
; involving vector-mediated recombinant protein gene  
transfer and expression in host cell for use in gene  
therapy  
AUTHOR: **SHEPPARD P O**; CHANDRASEKHER Y A  
PATENT ASSIGNEE: ZYMOGENETICS INC  
PATENT INFO: US 2002182677 5 Dec 2002  
APPLICATION INFO: US 2002-86135 26 Feb 2002  
PRIORITY INFO: US 2002-86135 26 Feb 2002; US 1998-95199 3 Aug 1998  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 2003-328618 [31]

L20 ANSWER 6 OF 49 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN  
ACCESSION NUMBER: 2003-13605 BIOTECHDS  
TITLE: Novel isolated **zsig63** polypeptide, member of the  
adhesin family, useful for treating dental carries,  
periodontal disease, thrush, gastrointestinal disease,  
urinary tract infections, vaginal infections, skin infections  
; vector-mediated gene transfer and expression in host cell  
for recombinant protein production for use in disease  
diagnosis and gene therapy  
AUTHOR: **ADLER D A**; **SHEPPARD P O**  
PATENT ASSIGNEE: ADLER D A; SHEPPARD P O  
PATENT INFO: US 2002173027 21 Nov 2002  
APPLICATION INFO: US 2001-922469 3 Aug 2001  
PRIORITY INFO: US 2001-922469 3 Aug 2001; US 1999-124820 17 Mar 1999  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 2003-328428 [31]

L20 ANSWER 7 OF 49 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN  
ACCESSION NUMBER: 2003-12930 BIOTECHDS  
TITLE: New **Zsig16** polypeptides, useful in immunological  
diagnostic assays for **Zsig16** gene expression;  
involving vector-mediated gene transfer and expression in  
bacterium, yeast, fungus, insect, mammal and plant cell  
for use in gene expression  
AUTHOR: **SHEPPARD P O**; HALDEMAN B A; HOLLY R D  
PATENT ASSIGNEE: ZYMOGENETICS INC

PATENT INFO: US 2002164764 7 Nov 2002  
APPLICATION INFO: US 2001-982405 18 Oct 2001  
PRIORITY INFO: US 2001-982405 18 Oct 2001; US 1998-100865 17 Sep 1998  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 2003-298699 [29]

L20 ANSWER 8 OF 49 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN  
ACCESSION NUMBER: 2003-11035 BIOTECHDS  
TITLE: New isolated **Zsig24** polypeptide and polynucleotides encoding the polypeptide, useful for diagnosing chromosome 11 abnormalities, or for diagnosing obesity or type II diabetes in an individual e.g., Pima Indian; recombinant protein production via vector expression in host cell

AUTHOR: SHEPPARD P O; JELINEK L J; WHITMORE T E  
PATENT ASSIGNEE: SHEPPARD P O; JELINEK L J; WHITMORE T E  
PATENT INFO: US 2002164701 7 Nov 2002  
APPLICATION INFO: US 2001-1631 25 Oct 2001  
PRIORITY INFO: US 2001-1631 25 Oct 2001; US 1998-105450 23 Oct 1998  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 2003-247256 [24]

L20 ANSWER 9 OF 49 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN  
ACCESSION NUMBER: 2003-08077 BIOTECHDS  
TITLE: New secretory protein-48 (**Zsig48**) polypeptides, useful for promoting proliferation of blood leukocytes and subsequently treating cancer patients whose leukocytes have been depleted by chemotherapy; vector-mediated gene transfer and expression in host cell for recombinant protein production, vaccine adjuvant and disease therapy

AUTHOR: LOK S; SHEPPARD P O; KINDSVOGEL W; BORT S J  
PATENT ASSIGNEE: ZYMOGENETICS INC  
PATENT INFO: US 2002132996 19 Sep 2002  
APPLICATION INFO: US 2001-955807 19 Sep 2001  
PRIORITY INFO: US 2001-955807 19 Sep 2001; US 1998-102679 1 Oct 1998  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 2003-155903 [15]

L20 ANSWER 10 OF 49 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN  
ACCESSION NUMBER: 2003-01837 BIOTECHDS  
TITLE: Novel secreted salivary polypeptide, **zsig63**, useful as antimicrobial agent for treating microbial infection, dental carries, periodontal disease, thrush gastrointestinal disease, and for aiding digestion; recombinant protein production and agonist and antagonist use in disease therapy and gene therapy

AUTHOR: ADLER D A; SHEPPARD P O  
PATENT ASSIGNEE: ADLER D A; SHEPPARD P O  
PATENT INFO: US 2002090677 11 Jul 2002  
APPLICATION INFO: US 2001-923236 3 Aug 2001  
PRIORITY INFO: US 2001-923236 3 Aug 2001; US 1999-124820 17 Mar 1999  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 2002-642378 [69]

L20 ANSWER 11 OF 49 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN  
ACCESSION NUMBER: 2003-01808 BIOTECHDS  
TITLE: Novel secreted salivary protein, **zsig63** and polynucleotide encoding it useful for treating microbial infections, inflammatory conditions, dental caries and lung

infections associated with cystic fibrosis;  
vector-mediated gene transfer and expression in host cell  
for recombinant protein production, drug screening and  
gene therapy

AUTHOR: ADLER D A; SHEPPARD P O  
PATENT ASSIGNEE: ADLER D A; SHEPPARD P O  
PATENT INFO: US 2002081701 27 Jun 2002  
APPLICATION INFO: US 2001-922480 3 Aug 2001  
PRIORITY INFO: US 2001-922480 3 Aug 2001; US 1999-124820 17 Mar 1999  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 2002-635468 [68]

L20 ANSWER 12 OF 49 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN

ACCESSION NUMBER: 2002-17104 BIOTECHDS

TITLE: ZSIG33-Like peptides and polynucleotides, useful  
for modulating gastric contractility, nutrient uptake, growth  
hormones and/or secretion of digestive/pancreatic enzymes and  
hormones;

vector-mediated recombinant protein gene transfer and  
expression in host cell for use in gene therapy,  
recombinant vaccine and nucleic acid vaccine preparation

AUTHOR: JASPERS S R; SHEPPARD P O; DEISHER T A; BISHOP P D  
PATENT ASSIGNEE: JASPERS S R; SHEPPARD P O; DEISHER T A; BISHOP P D  
PATENT INFO: US 2002055156 9 May 2002  
APPLICATION INFO: US 2000-853253 11 May 2000  
PRIORITY INFO: US 2001-853253 10 May 2001  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 2002-443750 [47]

L20 ANSWER 13 OF 49 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN

ACCESSION NUMBER: 2002-15389 BIOTECHDS

TITLE: New human ZSIG89 polypeptides and polynucleotides,  
useful for treating microbial infection, cancer, autoimmune  
disorders, bone disorders, inflammation, immunodeficiencies,  
wound, tumor, diabetes, pneumonia, asthma, emphysema and  
allergy;

vector-mediated gene transfer, expression in host cell,  
antisense oligonucleotide, DNA probe and DNA primer for  
recombinant protein production, drug screening and gene  
therapy

AUTHOR: ADLER D A; SHEPPARD P O; NELSON A J  
PATENT ASSIGNEE: ADLER D A; SHEPPARD P O; NELSON A J  
PATENT INFO: US 2002042095 11 Apr 2002  
APPLICATION INFO: US 1999-741711 21 Dec 1999  
PRIORITY INFO: US 2000-741711 19 Dec 2000  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 2002-315124 [35]

L20 ANSWER 14 OF 49 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN

ACCESSION NUMBER: 2003-14202 BIOTECHDS

TITLE: Novel isolated zsig45 polypeptide useful for  
treating or preventing disorders associated with thyroid  
dysfunction, inflammatory diseases, heart diseases,  
pancreatic disorders, atherosclerosis, restenosis, obesity;  
involving vector-mediated recombinant protein gene  
transfer and expression in host cell for use in disease  
prevention and therapy

AUTHOR: DEISHER T A; SHEPPARD P O  
PATENT ASSIGNEE: ZYMOGENETICS INC  
PATENT INFO: US 6500925 31 Dec 2002  
APPLICATION INFO: US 2000-522980 10 Mar 2000

PRIORITY INFO: US 2000-522980 10 Mar 2000; US 1997-67263 3 Dec 1997  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 2003-340475 [32]

L20 ANSWER 15 OF 49 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN  
ACCESSION NUMBER: 2003-12728 BIOTECHDS

TITLE: New antibody which binds to human thyroid protein,  
**zsig45**, useful for treating and preventing disorders  
associated with thyroid dysfunction and myocardial  
infarction, and also inflammatory disorders;  
monoclonal antibody production for disease diagnosis,  
therapy and prevention

AUTHOR: DEISHER T A; **SHEPPARD P O**  
PATENT ASSIGNEE: ZYMOGENETICS INC  
PATENT INFO: US 6486304 26 Nov 2002  
APPLICATION INFO: US 2000-523462 10 Mar 2000  
PRIORITY INFO: US 2000-523462 10 Mar 2000; US 1997-67263 3 Dec 1997  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 2003-298173 [29]

L20 ANSWER 16 OF 49 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN  
ACCESSION NUMBER: 2003-06033 BIOTECHDS

TITLE: Promoting blood flow within the vasculature of a mammal,  
comprises administering a pharmaceutical formulation  
comprising **zsig37** proteins;  
protein and agonist and antagonist use in disease gene  
therapy

AUTHOR: **SHEPPARD P O**; LASSER G W; BISHOP P D  
PATENT ASSIGNEE: ZYMOGENETICS INC  
PATENT INFO: US 6448221 10 Sep 2002  
APPLICATION INFO: US 2000-506855 17 Feb 2000  
PRIORITY INFO: US 2000-506855 17 Feb 2000; US 1999-253604 19 Feb 1999  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 2003-038245 [03]

L20 ANSWER 17 OF 49 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN  
ACCESSION NUMBER: 2002-19548 BIOTECHDS

TITLE: New isolated nucleic acid molecule encoding a tumor marker  
polypeptide, referred as **Zsig62**, useful for  
differentiating between normal and tumor tissues obtained  
from lung, uterus, breast, fallopian tube and ovary;  
recombinant protein production, antibody and transgenic  
mouse generation useful for tumor gene therapy and  
diagnosis

AUTHOR: **SHEPPARD P O**; NOVAK J E; RAYMOND F  
PATENT ASSIGNEE: ZYMOGENETICS INC  
PATENT INFO: US 6403783 11 Jun 2002  
APPLICATION INFO: US 1999-493565 19 Jan 1999  
PRIORITY INFO: US 2000-493565 18 Jan 2000  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 2002-556212 [59]

L20 ANSWER 18 OF 49 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN  
ACCESSION NUMBER: 2002-07489 BIOTECHDS

TITLE: New isolated **Zsig47** polypeptide useful in  
therapeutics and for detecting and modifying inflammation and  
immune response;  
vector-mediated recombinant protein gene transfer and  
expression in bacterium, yeast, fungus, insect, bird,  
mammal or plant cell for use in gene therapy

AUTHOR: SHEPPARD P O; GILBERT T  
PATENT ASSIGNEE: ZYMOGENETICS INC  
PATENT INFO: WO 2001090183 29 Nov 2001  
APPLICATION INFO: WO 2000-US16699 22 May 2000  
PRIORITY INFO: US 2000-206179 22 May 2000  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 2002-097643 [13]

L20 ANSWER 19 OF 49 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN  
ACCESSION NUMBER: 2002-06713 BIOTECHDS  
TITLE: New polypeptides; useful for modulating gastric contractility, nutrient uptake, pancreatic secretion of hormones, digestive enzymes and treating gastrointestinal and growth related diseases, comprises **zsig33**-like peptides;  
cancer, infection and metabolic disease, therapy and gene therapy

AUTHOR: JASPERS S R; SHEPPARD P O; DEISHER T A; BISHOP P D  
PATENT ASSIGNEE: ZYMOGENETICS INC  
PATENT INFO: WO 2001087933 22 Nov 2001  
APPLICATION INFO: WO 2000-US15091 11 May 2000  
PRIORITY INFO: US 2000-569271 11 May 2000  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 2002-082982 [11]

L20 ANSWER 20 OF 49 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN  
ACCESSION NUMBER: 2001-12940 BIOTECHDS  
TITLE: Novel secreted protein, **zsig87** polypeptides and polynucleotides for detecting human chromosomal abnormalities, as immunocontraceptives and for diagnosing, treating cancer, cardiovascular and inflammatory disease;  
recombinant protein gene production useful in gene therapy

AUTHOR: Sheppard P O  
PATENT ASSIGNEE: Zymogenetics  
LOCATION: Seattle, WA, USA.  
PATENT INFO: WO 2001042292 14 Jun 2001  
APPLICATION INFO: WO 2000-US33539 8 Dec 2000  
PRIORITY INFO: US 1999-456641 8 Dec 1999  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 2001-381639 [40]

L20 ANSWER 21 OF 49 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN  
ACCESSION NUMBER: 2001-11511 BIOTECHDS  
TITLE: Forming reversible peptide receptor complex for purifying cell and peptides, stimulating signal transduction and modulating hormone secretion, involves contacting a receptor with **zsig33** polypeptide;  
recombinant protein production for use in therapy

AUTHOR: Sheppard P O; Jaspers S R; Deisher T A; Bishop P D  
PATENT ASSIGNEE: Zymogenetics  
LOCATION: East Seattle, WA, USA.  
PATENT INFO: WO 2001038355 31 May 2001  
APPLICATION INFO: WO 2000-US32074 22 Nov 2000  
PRIORITY INFO: US 1999-166765 22 Nov 1999  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 2001-355879 [37]

L20 ANSWER 22 OF 49 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN  
ACCESSION NUMBER: 2002-08372 BIOTECHDS  
TITLE: New **zsig87** polynucleotides and encoded

polypeptides, useful for, e.g., studying pancreatic cell proliferation or differentiation, mammalian cellular metabolism, promoting wound healing, or treating cancers; vector-mediated recombinant protein gene transfer and expression in host cell, monoclonal antibody, agonist, antagonist, DNA probe and DNA primer for use in gene therapy

AUTHOR: SHEPPARD P O  
PATENT ASSIGNEE: SHEPPARD P O  
PATENT INFO: US 2001044134 22 Nov 2001  
APPLICATION INFO: US 1999-733523 8 Dec 1999  
PRIORITY INFO: US 2000-733523 8 Dec 2000  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 2002-105570 [14]

L20 ANSWER 23 OF 49 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN

ACCESSION NUMBER: 2002-08361 BIOTECHDS

TITLE: Polynucleotides encoding salivary proteins useful as anti-microbial agents; vector-mediated gene transfer and expression in host cell for recombinant protein production and gene therapy

AUTHOR: ADLER D A; SHEPPARD P O  
PATENT ASSIGNEE: ZYMOGENETICS INC  
PATENT INFO: US 6331413 18 Dec 2001  
APPLICATION INFO: US 1999-527345 17 Mar 1999  
PRIORITY INFO: US 2000-527345 17 Mar 2000  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 2002-096707 [13]

L20 ANSWER 24 OF 49 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN

ACCESSION NUMBER: 2000-12788 BIOTECHDS

TITLE: New member of the human secretin-glucagon-vasoactive intestinal peptide (VIP) family, designated Zsig67 polypeptide, useful as a diagnostic tool; vector-mediated gene transfer and expression in host cell and antibody

AUTHOR: Sheppard P O; Shoemaker K E; Tackett M L; Jaspers S R  
PATENT ASSIGNEE: Zymogenetics  
LOCATION: Seattle, WA, USA.  
PATENT INFO: WO 2000043516 27 Jul 2000  
APPLICATION INFO: WO 2000-US870 13 Jan 2000  
PRIORITY INFO: US 1999-233250 19 Jan 1999  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 2000-482913 [42]

L20 ANSWER 25 OF 49 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN

ACCESSION NUMBER: 2000-12328 BIOTECHDS

TITLE: Isolated polypeptide (P1) comprising an amino acid (aa) sequence at least 70% identical to Zsig62 specifically binds with an antibody that specifically binds to Zsig62; tumor marker and antibody for use in mamma cancer and prostate cancer diagnosis and prognosis

AUTHOR: Sheppard P O; Novak J E; Raymond F C  
PATENT ASSIGNEE: Zymogenetics  
LOCATION: East Seattle, WA, USA.  
PATENT INFO: WO 2000042183 20 Jul 2000  
APPLICATION INFO: WO 2000-US1902 18 Jan 2000  
PRIORITY INFO: US 1999-233610 19 Jan 1999  
DOCUMENT TYPE: Patent

LANGUAGE: English  
OTHER SOURCE: WPI: 2000-466129 [40]

L20 ANSWER 26 OF 49 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN  
ACCESSION NUMBER: 2000-12126 BIOTECHDS  
TITLE: Nucleic acids encoding pancreatic **zsig66** proteins  
useful for identifying compounds that may be used to treat,  
for example microbial infections;  
recombinant protein production for e.g. ovary, eye, blood  
and bone disorder therapy and diagnosis  
AUTHOR: Sheppard P O  
PATENT ASSIGNEE: Zymogenetics  
LOCATION: Seattle, WA, USA.  
PATENT INFO: WO 2000036104 22 Jun 2000  
APPLICATION INFO: WO 1999-US29669 14 Dec 1999  
PRIORITY INFO: US 1998-212947 16 Dec 1998  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 2000-475395 [41]

L20 ANSWER 27 OF 49 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN  
ACCESSION NUMBER: 2000-11614 BIOTECHDS  
TITLE: Novel G-protein coupled receptor **zsig56** useful for  
treating hypertension, hyper and hypothyroidism,  
inflammation, gout, carcinoma, pancreatitis, Alzheimer  
disease and Parkinson disease, renal and heart failure;  
vector-mediated gene transfer and expression in host cell,  
antibody, anti-idiotypic antibody DNA probe and DNA primer  
AUTHOR: Sheppard P O; Ellsworth J L  
PATENT ASSIGNEE: Zymogenetics  
LOCATION: Seattle, WA, USA.  
PATENT INFO: WO 2000034473 15 Jun 2000  
APPLICATION INFO: WO 1999-US28492 2 Dec 1999  
PRIORITY INFO: US 1998-208691 10 Dec 1998  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 2000-424164 [36]

L20 ANSWER 28 OF 49 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN  
ACCESSION NUMBER: 2000-10594 BIOTECHDS  
TITLE: Isolated **Zsig43** polypeptides and nucleic acids  
useful for detecting **Zsig43** gene expression in  
samples and for screening for modulators of **Zsig43**  
activity;  
vector-mediated gene transfer and expression in bacterium,  
yeast, fungus or mammal host cell, antibody and DNA probe  
AUTHOR: Sheppard P O; Lok S  
PATENT ASSIGNEE: Zymogenetics  
LOCATION: Seattle, WA, USA.  
PATENT INFO: WO 2000031259 2 Jun 2000  
APPLICATION INFO: WO 1999-US27040 15 Nov 1999  
PRIORITY INFO: US 1998-200417 23 Nov 1998  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 2000-400069 [34]

L20 ANSWER 29 OF 49 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN  
ACCESSION NUMBER: 2000-10043 BIOTECHDS  
TITLE: Mammalian secretory protein-61 for gene therapy of various  
disorders such as autoimmune diseases;  
involving electroporation-mediated gene transfer,  
expression in DH10B cell  
AUTHOR: Sheppard P O  
PATENT ASSIGNEE: Zymogenetics

LOCATION: Seattle, WA, USA.  
PATENT INFO: WO 2000028030 18 May 2000  
APPLICATION INFO: WO 1999-US26585 9 Nov 1999  
PRIORITY INFO: US 1998-191074 12 Nov 1998  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 2000-376544 [32]

L20 ANSWER 30 OF 49 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN

ACCESSION NUMBER: 2000-09265 BIOTECHDS

TITLE: **Zsig49** Polypeptides and polynucleotides, useful for treatment and diagnosis of metabolic diseases such as diabetes;  
vector-mediated gene transfer and expression in host cell, antibody and anti-idiotypic antibody for gene therapy

AUTHOR: **Sheppard P O**; Holly R D; Gao Z; Whitmore T E; Maurer M F

PATENT ASSIGNEE: Zymogenetics

LOCATION: Seattle, WA, USA.

PATENT INFO: WO 2000023591 27 Apr 2000

APPLICATION INFO: WO 1999-US24579 20 Oct 1999

PRIORITY INFO: US 1998-176545 21 Oct 1998

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2000-339690 [29]

L20 ANSWER 31 OF 49 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN

ACCESSION NUMBER: 2000-08478 BIOTECHDS

TITLE: Human secretory protein 48 polypeptides and polynucleotides useful for promoting leukocyte proliferation and for treating immunosuppressed individuals;  
production of protein, **Zsig48**, via vector useful for treating cancer and HIV virus-1 infection

AUTHOR: Lok S; **Sheppard P O**

PATENT ASSIGNEE: Zymogenetics

LOCATION: Seattle, WA, USA.

PATENT INFO: WO 2000018796 6 Apr 2000

APPLICATION INFO: WO 1999-US22970 1 Oct 1999

PRIORITY INFO: US 1998-164740 1 Oct 1998

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2000-303441 [26]

L20 ANSWER 32 OF 49 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN

ACCESSION NUMBER: 2000-06498 BIOTECHDS

TITLE: New polynucleotide encoding a member of trabecular meshwork-induced glucocorticoid response protein for treating ovarian, pancreatic, ocular, blood and bone disorders such as osteoporosis and Paget's disease;  
expression in host cell, monoclonal antibody, transgenic mouse, DNA probe and DNA primer

AUTHOR: **Sheppard P O**; Chandrasekher Y

PATENT ASSIGNEE: Zymogenetics

LOCATION: Seattle, WA, USA.

PATENT INFO: WO 2000008154 17 Feb 2000

APPLICATION INFO: WO 1999-US17552 3 Aug 1999

PRIORITY INFO: US 1998-128372 3 Aug 1998

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2000-205709 [18]

L20 ANSWER 33 OF 49 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN

ACCESSION NUMBER: 2001-04815 BIOTECHDS

TITLE: New isolated serine protease (designated **Zsig13**),



useful in industrial processes to degrade unwanted proteins or alter the characteristics of protein-containing composition, as well as in industrial applications (e.g. brewing);

enzyme production using an expression vector system

AUTHOR: Sheppard P O  
PATENT ASSIGNEE: Zymogenetics  
LOCATION: Seattle, WA, USA.  
PATENT INFO: US 6153420 28 Nov 2000  
APPLICATION INFO: US 1998-72384 4 May 1998  
PRIORITY INFO: US 1998-72384 4 May 1998  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 2001-060090 [07]

L20 ANSWER 34 OF 49 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN  
ACCESSION NUMBER: 2001-03858 BIOTECHDS

TITLE: New **zsig45** polypeptides and polynucleotides for treating or preventing e.g. thyroid, bone or heart disorders, inflammation, cancer, viral and bacterial infections;  
human recombinant **zsig45** protein gene useful in gene therapy

AUTHOR: Deisher T A; Sheppard P O  
PATENT ASSIGNEE: ZymoGenetics  
LOCATION: Seattle, WA, USA.  
PATENT INFO: US 6140084 31 Oct 2000  
APPLICATION INFO: US 1998-203623 1 Dec 1998  
PRIORITY INFO: US 1998-203623 1 Dec 1998  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 2001-040302 [05]

L20 ANSWER 35 OF 49 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN  
ACCESSION NUMBER: 2000-03582 BIOTECHDS

TITLE: Polynucleotides encoding the polypeptide **zsig57** useful for regulating the immune system;  
recombinant protein production via vector-mediated gene transfer and expression in host cell for e.g. asthma and arthritis diagnosis, therapy and gene therapy

AUTHOR: Sheppard P O  
PATENT ASSIGNEE: Zymogenetics  
LOCATION: Seattle, WA, USA.  
PATENT INFO: WO 9966040 23 Dec 1999  
APPLICATION INFO: WO 1999-US11337 20 May 1999  
PRIORITY INFO: US 1998-99600 18 Jun 1998  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 2000-097745 [08]

L20 ANSWER 36 OF 49 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN  
ACCESSION NUMBER: 1999-13810 BIOTECHDS

TITLE: Novel cystine knot family member **zsig51**, useful for diagnosing cell proliferation disorders e.g. cancer in pancreatic, pituitary, testicular or eye tissue;  
recombinant protein production via vector-mediated gene transfer and expression in host cell and antibody, DNA probe and DNA primer for cancer diagnosis and therapy

AUTHOR: Sheppard P O; Lok S  
PATENT ASSIGNEE: Zymogenetics  
LOCATION: Seattle, WA, USA.  
PATENT INFO: WO 9941377 19 Aug 1999  
APPLICATION INFO: WO 1999-US3104 12 Feb 1999  
PRIORITY INFO: US 1998-23570 13 Feb 1998  
DOCUMENT TYPE: Patent

LANGUAGE: English  
OTHER SOURCE: WPI: 1999-518449 [43]

L20 ANSWER 37 OF 49 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN  
ACCESSION NUMBER: 1999-10865 BIOTECHDS  
TITLE: New human thyroid **ZSIG45** DNA;  
expression in host cell, fusion protein and antibody used  
for thyroid-related condition diagnosis, therapy and drug  
screening  
AUTHOR: **Sheppard P O**; Deisher T A  
PATENT ASSIGNEE: Zymogenetics  
LOCATION: Seattle, WA, USA.  
PATENT INFO: WO 9928467 10 Jun 1999  
APPLICATION INFO: WO 1998-US25454 1 Dec 1998  
PRIORITY INFO: US 1997-984638 3 Dec 1997  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 1999-371121 [31]

L20 ANSWER 38 OF 49 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN  
ACCESSION NUMBER: 1999-08092 BIOTECHDS  
TITLE: Polynucleotide encoding a human secretory protein,  
**ZSIG-II**;  
expression in host cell, antibody, anti-idiotypic antibody  
and antagonist used for fertility inducement  
AUTHOR: **Sheppard P O**  
PATENT ASSIGNEE: Zymogenetics  
LOCATION: Seattle, WA, USA.  
PATENT INFO: WO 9916870 8 Apr 1999  
APPLICATION INFO: WO 1998-US20449 29 Sep 1998  
PRIORITY INFO: US 1998-85966 19 May 1998; US 1997-60327 29 Sep 1997  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 1999-263692 [22]

L20 ANSWER 39 OF 49 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN  
ACCESSION NUMBER: 1999-06705 BIOTECHDS  
TITLE: **Zsig39** protein;  
and nucleic acid used to metabolize fatty acid in ischemia  
and inflammation prevention, organ cryopreservation, and  
as an antibiotic  
AUTHOR: **Sheppard P O**; Humes J M  
PATENT ASSIGNEE: Zymogenetics  
LOCATION: Seattle, WA, USA.  
PATENT INFO: WO 9910492 4 Mar 1999  
APPLICATION INFO: WO 1998-US17724 26 Aug 1998  
PRIORITY INFO: US 1997-56983 26 Aug 1997  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 1999-204665 [17]

L20 ANSWER 40 OF 49 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN  
ACCESSION NUMBER: 1999-04706 BIOTECHDS  
TITLE: A new polypeptide encoding the human chloride ion channel,  
**zsig44**;  
expression in host cell and antibody used for diabetes,  
bone disease or leukemia therapy and gene therapy, etc.  
AUTHOR: **Sheppard P O**; Moore E E  
PATENT ASSIGNEE: Zymogenetics  
LOCATION: Seattle, WA, USA.  
PATENT INFO: WO 9905276 4 Feb 1999  
APPLICATION INFO: WO 1998-US15493 24 Jul 1998  
PRIORITY INFO: US 1997-53715 25 Jul 1997  
DOCUMENT TYPE: Patent

LANGUAGE: English  
OTHER SOURCE: WPI: 1999-142931 [12]

L20 ANSWER 41 OF 49 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN  
ACCESSION NUMBER: 1999-04705 BIOTECHDS  
TITLE: New secreted polypeptide, **zsig46**, and its  
fragments, related fusion proteins;  
vector plasmid zsig46CEE/pZP9-mediated expression in  
Escherichia coli, antibody and antisense sequence used for  
thyroid disease therapy, gene therapy and transgenic  
animal, etc.  
AUTHOR: **Sheppard P O**; Gilbertson D G  
PATENT ASSIGNEE: Zymogenetics  
LOCATION: Seattle, WA, USA.  
PATENT INFO: WO 9905275 4 Feb 1999  
APPLICATION INFO: WO 1998-US15431 24 Jul 1998  
PRIORITY INFO: US 1997-53613 24 Jul 1997  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 1999-142930 [12]

L20 ANSWER 42 OF 49 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN  
ACCESSION NUMBER: 1999-04674 BIOTECHDS  
TITLE: New isolated adipocyte complement related polypeptides;  
nucleic acid, expression vector, antibody, DNA probe and  
DNA primer used for disease diagnosis, therapy, gene  
therapy and drug screening  
AUTHOR: **Sheppard P O**  
PATENT ASSIGNEE: Zymogenetics  
LOCATION: Seattle, WA, USA.  
PATENT INFO: WO 9904000 28 Jan 1999  
APPLICATION INFO: WO 1998-US14864 17 Jul 1998  
PRIORITY INFO: US 1997-53154 18 Jul 1997  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 1999-132244 [11]

L20 ANSWER 43 OF 49 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN  
ACCESSION NUMBER: 1999-04029 BIOTECHDS  
TITLE: New mammalian secretory peptide-9 (**Zsig9**);  
antibody or antisense molecule, used for cancer therapy  
and placenta, heart or liver development  
AUTHOR: **Sheppard P O**; Jelinek L J; Jaspers S R; Whitmore T  
E  
PATENT ASSIGNEE: Zymogenetics  
LOCATION: Seattle, WA, USA.  
PATENT INFO: WO 9901554 14 Jan 1999  
APPLICATION INFO: WO 1998-US13859 2 Jul 1998  
PRIORITY INFO: US 1998-99005 17 Jun 1998; US 1997-51704 3 Jul 1997  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 1999-106055 [09]

L20 ANSWER 44 OF 49 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN  
ACCESSION NUMBER: 1999-02075 BIOTECHDS  
TITLE: New nucleic acid encoding secreted polypeptide **zsig15**  
;  
plasmid expression in BHK cell and fusion peptide,  
antibody, DNA probe and DNA primer for e.g. cancer gene  
therapy, antisense therapy  
AUTHOR: **Sheppard P O**; Grossman A  
PATENT ASSIGNEE: Zymogenetics  
LOCATION: Seattle, WA, USA.  
PATENT INFO: WO 9850552 12 Nov 1998

APPLICATION INFO: WO 1998-US9584 6 May 1998  
PRIORITY INFO: US 1997-45703 6 May 1997  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 1999-034723 [03]

L20 ANSWER 45 OF 49 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN  
ACCESSION NUMBER: 1999-00136 BIOTECHDS  
TITLE: New szig-25 protein and related DNA sequences, fusion proteins, vectors, transformed cells, antibody;  
involved in modulation of adhesion, used for diagnosis and treatment of prostatic and B-lymphocyte tumors, stimulation of hematopoietic cells, treatment of immune deficiency, etc.  
AUTHOR: Sheppard P O  
PATENT ASSIGNEE: Zymogenetics  
LOCATION: Seattle, WA, USA.  
PATENT INFO: WO 9845442 15 Oct 1998  
APPLICATION INFO: WO 1998-US7117 10 Apr 1998  
PRIORITY INFO: US 1997-49288 11 Jun 1997; US 1997-43421 10 Apr 1997  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 1998-557522 [47]

L20 ANSWER 46 OF 49 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN  
ACCESSION NUMBER: 1999-00123 BIOTECHDS  
TITLE: New human chemokine ZSIG-35;  
vector-mediated gene transfer and expression in host cell, antibody, DNA probe and DNA primer, used for inflammatory disease, lymphocyte migration and reperfusion injury therapy  
AUTHOR: Sheppard P O  
PATENT ASSIGNEE: Zymogenetics  
LOCATION: Seattle, WA, USA.  
PATENT INFO: WO 9844117 8 Oct 1998  
APPLICATION INFO: WO 1998-US6115 27 Mar 1998  
PRIORITY INFO: US 1997-46083 9 May 1997; US 1997-42862 28 Mar 1997  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 1998-557114 [47]

L20 ANSWER 47 OF 49 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN  
ACCESSION NUMBER: 1999-02656 BIOTECHDS  
TITLE: Human polypeptide having homology to motilin, zsig33\*\*\*;  
used in the treatment of gastric disorders and as obesity therapy  
AUTHOR: \*\*\*Sheppard P O; Deisher T A  
PATENT ASSIGNEE: Zymogenetics  
LOCATION: Seattle, WA, USA.  
PATENT INFO: WO 9842840 1 Oct 1998  
APPLICATION INFO: WO 1998-US5620 23 Mar 1998  
PRIORITY INFO: US 1997-41102 24 Mar 1997; US 1997-822897 24 Mar 1997  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 1999-070071 [06]

L20 ANSWER 48 OF 49 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN  
ACCESSION NUMBER: 1998-11207 BIOTECHDS  
TITLE: Recombinant zsig-32 protein involved in salivary gland and mucous associated functions;  
used in the drug screening, diagnosis and treatment of a range of lung, salivary gland, etc. disorder  
AUTHOR: Sheppard P O  
PATENT ASSIGNEE: Zymogenetics

LOCATION: Seattle, WA, USA.  
PATENT INFO: WO 9841628 24 Sep 1998  
APPLICATION INFO: WO 1998-US5255 18 Mar 1998  
PRIORITY INFO: US 1997-41263 19 Mar 1997  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 1998-531567 [45]

L20 ANSWER 49 OF 49 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN  
ACCESSION NUMBER: 1998-11206 BIOTECHDS  
TITLE: Secreted novel **zsig**-10 protein;  
with homology to the Xenopus cement gland protein used in  
the treatment, diagnosis and drug screening of a range of  
diseases e.g. cancer, bacterium infection, AIDS, etc.

AUTHOR: Sheppard P O  
PATENT ASSIGNEE: Zymogenetics  
LOCATION: Seattle, WA, USA.  
PATENT INFO: WO 9841627 24 Sep 1998  
APPLICATION INFO: WO 1998-US5251 18 Mar 1998  
PRIORITY INFO: US 1997-39631 19 Mar 1997  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 1998-531566 [45]

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FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,  
LIFESCI' ENTERED AT 11:45:38 ON 30 JAN 2004

L1 6 S "ZSIG63"  
L2 4 DUP REM L1 (2 DUPLICATES REMOVED)  
L3 146427 S SALIVARY  
L4 150 S ZSIG###  
L5 12 S L3 AND L4  
L6 8 DUP REM L5 (4 DUPLICATES REMOVED)  
L7 6346882 S CLON? OR EXPRESS? OR RECOMBINANT  
L8 126 S L4 AND L7  
L9 100 S HUMAN AND L8  
L10 23 S CANCER AND L9  
L11 23517 S TRANSCRIPTION(A) ACTIVATION OR ANTI(W) MICROBIAL  
L12 4 S L9 AND L11  
L13 23517 S L11 OR L12  
L14 26 S L12 OR L10  
L15 21 DUP REM L14 (5 DUPLICATES REMOVED)  
E ADLER D A/AU  
L16 233 S E3  
E SHEPPARD P O/AU  
L17 194 S E3  
L18 422 S L16 OR L17  
L19 49 S L4 AND L18  
L20 49 DUP REM L19 (0 DUPLICATES REMOVED)  
L21 4 S L1 AND L20  
L22 4 DUP REM L21 (0 DUPLICATES REMOVED)

	Issue Date	Pages	Document ID	Title
1	20021121	32	US 20020173027 A1	Secreted salivary zsig63 polypeptide
2	20020711	33	US 20020090677 A1	Secreted salivary zsig63 polypeptide
3	20020627	33	US 20020081701 A1	Secreted salivary zsig63 polypeptide
4	20011218	29	US 6331413 B1	Secreted salivary ZSIG63 Polypeptide

	Issue Date	Pages	Document ID	Title
1	20040122	42	US 20040014650 A1	Methods for enhancing wound repair
2	20031127	40	US 20030220253 A1	Inhibitors for use in hemostasis
3	20030918	40	US 20030176645 A1	Secreted salivary zsig32 polypeptides
4	20030731	48	US 20030144208 A1	Inhibitors for use in hemostasis and immune function
5	20030424	43	US 20030078206 A1	Inhibitors for use in hemostasis and immune function
6	20030130	46	US 20030022838 A1	Methods for pacifying the surface of a prosthetic biomaterial
7	20021219	46	US 20020192777 A1	Testis protein, Zsig86
8	20021121	32	US 20020173027 A1	Secreted salivary zsig63 polypeptide
9	20020711	33	US 20020090677 A1	Secreted salivary zsig63 polypeptide
10	20020627	39	US 20020082393 A1	SECRETED SALIVARY ZSIG32 POLYPEPTIDES
11	20020627	33	US 20020081701 A1	Secreted salivary zsig63 polypeptide
12	20020411	32	US 20020042095 A1	Secreted protein, ZSIG89
13	20030408	44	US 6544946 B1	Inhibitors for use in hemostasis and immune function

	Issue Date	Pages	Document ID	Title
14	20020910	39	US 6448221 B1	Methods of promoting blood flow within the vasculature of a mammal
15	20011218	29	US 6331413 B1	Secreted salivary ZSIG63 Polypeptide
16	20000215	37	US 6025197 A	Secreted salivary zsig32 polypeptides
17	20000208	36	US 6022847 A	Secreted salivary zsig32 polypeptides



	Issue Date	Pages	Document ID	Title
1	20021121	32	US 20020173027 A1	Secreted salivary zsig63 polypeptide
2	20020711	33	US 20020090677 A1	Secreted salivary zsig63 polypeptide
3	20020627	33	US 20020081701 A1	Secreted salivary zsig63 polypeptide
4	20011218	29	US 6331413 B1	Secreted salivary ZSIG63 Polypeptide

	Issue Date	Pages	Document ID	Title
1	20040129	36	US 20040018549 A1	Human secreted protein, Zsig47
2	20040122	42	US 20040014650 A1	Methods for enhancing wound repair
3	20031225	25	US 20030235887 A1	TML polynucleotides
4	20030918	46	US 20030176659 A1	Adipocyte-specific protein homologs
5	20030918	46	US 20030176658 A1	Adipocyte-specific protein homologs
6	20030918	40	US 20030176645 A1	Secreted salivary zsig32 polypeptides
7	20030918	26	US 20030176640 A1	SGIP peptides
8	20030911	49	US 20030171547 A1	Adipocyte-specific protein homologs
9	20030911	26	US 20030171542 A1	Mammalian secretory peptide - 9
10	20030904	41	US 20030166156 A1	Zsig67: a member of the human secretin-glucagon-VIP hormone family
11	20030904	36	US 20030166049 A1	Human secreted protein, Zsig47

	Issue Date	Pages	Document ID	Title
12	20030807	41	US 20030148357 A1	Novel cystine knot protein and materials and methods for making it
13	20030731	48	US 20030144208 A1	Inhibitors for use in hemostasis and immune function
14	20030710	43	US 20030129698 A1	Adipocyte complement related protein homolog zacrp7
15	20030605	52	US 20030104602 A1	Adipocyte complement related protein zacrp3X2
16	20030424	43	US 20030078206 A1	Inhibitors for use in hemostasis and immune function
17	20030130	46	US 20030022838 A1	Methods for pacifying the surface of a prosthetic biomaterial
18	20021226	38	US 20020197620 A1	Tumor marker Zsig62
19	20021219	46	US 20020192777 A1	Testis protein, Zsig86
20	20021205	49	US 20020182677 A1	Pancreatic and ovarian polypeptide, zsig58
21	20021121		US 20020173624 A1	Secreted proteins encoded by human chromosome 13
22	20021121	32	US 20020173027 A1	Secreted salivary zsig63 polypeptide

	Issue Date	Pages	Document ID	Title
23	20021107		US 20020164764 A1	Transmembrane polypeptide expressed by lymphocytes
24	20021107	34	US 20020164701 A1	Human gene marker for metabolic disease
25	20021024		US 20020156243 A1	Adipocyte-specific protein homologs
26	20020919		US 20020132996 A1	Secretory protein-48
27	20020711	33	US 20020090677 A1	Secreted salivary zsig63 polypeptide
28	20020704		US 20020086367 A1	Novel secreted proteins
29	20020627	39	US 20020082393 A1	SECRETED SALIVARY ZSIG32 POLYPEPTIDES
30	20020627	33	US 20020081701 A1	Secreted salivary zsig63 polypeptide
31	20020509		US 20020055156 A1	Zsig33-like peptides
32	20020411	32	US 20020042095 A1	Secreted protein, ZSIG89
33	20020411		US 20020042093 A1	SECRETED PROTEINS ENCODED BY HUMAN CHROMOSOME 13

	Issue Date	Pages	Document ID	Title
34	20011122		US 20010044134 A1	Novel secreted polypeptide zsig87
35	20011115		US 20010041791 A1	Motilin homologs
36	20030930		US 6627729 B1	TML peptides
37	20030603		US 6573363 B1	Cystine knot protein and materials and methods for making it
38	20030520		US 6566499 B1	Adipocyte-specific protein homologs
39	20030408	44	US 6544946 B1	Inhibitors for use in hemostasis and immune function
40	20030211		US 6518403 B2	Antibodies that bind an adipocyte-specific protein homolog
41	20021231		US 6500925 B1	Human thyroid protein ZSIG45
42	20021126		US 6486304 B1	Antibodies and methods of making antibodies to human thyroid protein zsig45

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43	20021119		US 6482612 B1	Adipocyte-specific protein homologs
44	20020910	39	US 6448221 B1	Methods of promoting blood flow within the vasculature of a mammal
45	20020716		US 6420521 B1	Short gastrointestinal peptides
46	20020611		US 6403783 B1	Nucleic acid which encodes the tumor marker ZSIG62
47	20020430		US 6380158 B1	Motilin homologs
48	20011218	29	US 6331413 B1	Secreted salivary ZSIG63 Polypeptide
49	20010918		US 6291653 B1	Antibodies to motilin homologs
50	20010724		US 6265544 B1	Adipocyte-specific protein homologs

	Issue Date	Pages	Document ID	Title
51	20010306		US 6197930 B1	Adipocyte-specific protein homologs
52	20001128		US 6153420 A	Serine protease polypeptides and materials and methods for making them
53	20001031		US 6140084 A	Human thyroid protein zsig45
54	20000704		US 6084088 A	Polynucleotides encoding novel tumor antigens
55	20000215	37	US 6025197 A	Secreted salivary zsig32 polypeptides
56	20000208	36	US 6022847 A	Secreted salivary zsig32 polypeptides

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2	L2	4	"zsig63"
3	L3	6750	salivary
4	L4	131	zsig\$3
5	L5	17	l3 same l4
6	L6	595126	clon\$3 or express\$3 or recombinant
7	L7	17	l5 same l6
8	L8	389872	human
9	L9	73	l4 same l8
10	L10	10094	transcription adj activation or anti adj microbial.
11	L11	4	l9 same l10
12	L12	1549	adler.in.



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14	L14	2702	l12 or l13
15	L15	53	l9 and l14
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17	L17	53	l9 and l14